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THE STABLER-LEADBEATER PHARMACY—NOW A MUSEUM.

This pharmacy, 107 S. Fairfax Street, Alexandria, Va., was established in 1792 by Edward Stabler, a Quaker, on a borrowed capital of 100 pounds or less than $500.00. The original stock and equipment, including about 150 items, came from London through Townsend Speakman of Philadelphia and cost approximately 120 pounds. The original bill, dated June 1792, has been preserved and three of the items of equipment mentioned have been in constant use, notably the bottle labeled, "Spt. Nitre." The loan was repaid within one year and the pharmacy was conducted by Mr. Stabler and his family successors until 1933, or a period of 141 years when the last descendant, Mr. Edward Stabler-Leadbeater, died and the pharmacy was sold to close the estate. It was not closed during the War of 1812 or during the Civil War. An interesting chronological history of the institution will be found in the JOUR. A. PH. A., for April 1934.

Through this continuous family ownership the original fixtures and equipment and the progressive records were preserved to a remarkable degree. The pharmacy was patronized by many of the distinguished families who lived in or near Alexandria, including the Washingtons, Lees and Masons, to name a few. Its proximity to Washington brought into its patronage also many outstanding citizens whose names are household words in every section of our country. Because its existence practically parallels that of the United States, because of the great events which took place in or around it and because of the great men and women who were its patrons, this pharmacy is a veritable storehouse of historical material, pharmaceutical and otherwise.

When the pharmacy was disposed of in 1933, the stock, equipment and records were purchased through friends, including L. Manuel Hendler and others, and their preservation was assured. Later, the Landmarks Society of Alexandria bought the original building in which the pharmacy was conducted and the one adjoining. The Society has had the coöperation of many persons who were interested in having the buildings preserved, and they have been faithfully restored to their original condition. It was understood that if the buildings were restored and

a plan to conduct the pharmacy as a museum was developed the stock equipment and records would be left as they were. The members of the Landmarks Society have arranged for the careful supervision of the museum and to support it by the proceeds from a Gift Shop conducted in the adjoining building.

The buildings are gems of Colonial architecture. The glazed doors which are original had lain in the attic for many years as had the curved mahogany shutters which were put up and taken down each day. The circular and paned windows were designed to display the apothecary's showglobes. The quaint and dignified interior of the pharmacy has been repainted in the original colors but otherwise remains unchanged. Busts of Washington and Franklin are located on either side of the arch in the rear. On the counter to the left can be seen the General Robert E. Lee plate. Here the great leader stood visiting with the then owner, Mr. Leadbeater, when J. E. B. Stuart, later the noted cavalry chieftain, brought to him the news of the John Brown raid and orders to proceed to Harpers Ferry to quell the rebellion.

The entire stock of furnishings is authentic and belonged to the pharmacy. Hundreds of hand-blown medicinal bottles, old scales with the royal crown, castor oil feeders, "Perfection" eyeglasses, little wooden medicine chests fully equipped, mortars and pestles of every size (the largest mortar measures two feet across, and one has to stand in order to use the pestle), are among the many relics to be seen. The documentary records are probably without equal in any pharmacy in America. Bales and bales of them are preserved, and it is interesting to speculate on what a careful study of them will bring to light.

The Stabler-Leadbeater Pharmacy is a definite part of the Historical Museum in the American Institute of Pharmacy. It is located within a short drive from the Institute. Here one can visit, in its original setting, a Colonial pharmacy, fully representative of that period and one that has been conducted during the intervening years by members of the same family. It is truly a connecting link with the past and speaks eloquently of what pharmacy meant in those days. Against this permanent background, the Historical Museum can depict what has happened to the profession in the meantime.

The old clock at the back of the store has run all this time and is still ticking away. It is hoped that the people of America, and particularly the pharmacists, will come to Alexandria to visit the Stabler-Leadbeater Pharmacy, to relive a chapter from the past, and to recapture the spirit of the early days when the great and near-great came and went through its doors.—E. F. K.

D. C. FAIR TRADE BILL.

The District of Columbia Fair Trade Bill, H. R. 3838, was passed by the House of Representatives on June 12th, without debate or objection. This is the second time the House has passed such a measure within a year. The bill was sent to the Senate and was there referred to the District Committee of which Senator King, of Utah, was chairman. It is expected that the bill will have early attention by the Committee and will be reported to the Senate in time for action during this session of Congress.

EDITORIAL

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HOSPITAL PHARMACY.

AT THE recent meeting of the American Medical Association in St. Louis, the Council on Medical Education and Hospitals submitted a revised list of "Essentials of a Registered Hospital" which was approved with some amendments. In addition to a general statement the essentials are listed under ten headings, as follows:

Organization, Physical Plant, Medical Staff, Pathology and Laboratory Diagnosis, Autopsies, Radiology, Anesthesia, Nursing Service, Dietetics, Pharmacy, Medical Records and Ethics.

The following wording applies to Pharmacy: "The handling of drugs should be properly supervised and should comply with all legal regulations. Accurate records should be maintained. A qualified person should be placed in charge, preferably a registered pharmacist; whatever arrangement is made, all prescriptions should be filled by a graduate pharmacist."

These requirements are more specific and comprehensive than those formerly in effect and their observance should lead to a decided improvement in the pharmaceutical service rendered in the registered hospitals of the country.—E. F. K.

THE DRIVE AGAINST GONORRHEA.

AT THE New York meeting of the ASSOCIATION in 1937, Acting Surgeon General Draper gave a very complete outline of the plans of the U. S. Public Health Service to banish venereal diseases and advised the pharmacists of the nation what they should and should not do to aid the program.

An Advisory Committee to the Service later submitted Recommendations for a Gonorrhea Control Program and they were published in the January 1938 issue of the U. S. Public Health Service Pamphlet, copy of which may be obtained from the Service.

In the report it was stated that, "It is the opinion of the committee that if full utilization were made of our present knowledge, the available diagnostic and therapeutic armamentarium would suffice for the control of gonorrhea as a public health problem. The public should be taught the cause and nature of gonorrhea, the essential facts concerning its prevalence and epidemiology, how it may be prevented, the reasons for treatment and what can be accomplished in terms of cure."

Pharmacists have been and can continue to be of great assistance in the program against venereal diseases and, in so doing, emphasize the important part they take in protecting and promoting public health. In this activity pharmacists can amply justify the statement made in the Charter's report that, "A well-informed pharmacist is the best single individual to disseminate information about public health."—E. F. K.

INTERNATIONAL CONGRESS OF MILITARY MEDICINE AND PHARMACY.

THE OFFICIAL sessions and entertainment features of the Tenth International Congress, referred to on page 265 of the May issue of the JOURNAL, were very successful and enjoyable. They were conducted in a manner thoroughly creditable to the officials of the United States who were responsible for the arrangements and for the comfort of the distinguished visitors from other countries, under the direction of Surgeon General Charles R. Reynolds, the President and Colonel Harold W. Jones, the Secretary General of the Congress.

The pharmaceutical delegates took part in all of the sessions and functions. Of special interest was the Sectional Meeting on Tuesday afternoon, May 9th, devoted to the Organization and Function of the Chemico-Pharmaceutical Service. Colonel Jules Thomann, chief pharmacist of the Swiss Army, presided and the following delegates presented papers. Dr. Ramon Antonio Alcaraz, principal pharmacist of the Argentine Army; Colonel Jareslav Janda of the Czechoslovakian Army; Colonel Thomann of the Swiss Army; Pharmacist Captain J. Raton, of the French Army; Pharmacist Major (Reserve) Isadore Elienne of the Belgium Army. This meeting was attended by a number of pharmacists from Washington and by President Lascoff of the AMERICAN PHARMACEUTICAL ASSOCIATION, who spoke for the ASSOCIATION.

On Tuesday evening, the pharmaceutical delegates, with President Lascoff and Secretary Kelly, of the A. PH. A., were entertained at dinner at the Willard Hotel by the members of the Executive Committee of the District of Columbia Pharmaceutical Association.

Practically all of the pharmaceutical delegates found time during their busy stay in Washington to visit the Pharmacy Building, to inspect the work being carried on by the ASSOCIATION, and to secure information about pharmaceutical conditions in this country.

The profession of Pharmacy was given recognition by the Congress in the election of Colonel Jules Thomann as president, to serve during the coming two years and to preside over the Eleventh Congress which will be held in Switzerland in 1941. Colonel Thomann has taken an active part in the work of the Congress, has served recently on its Permanent Committee and has had a distinguished career in the Swiss Army of which he is now the chief pharmacist. The President of the Congress, upon the completion of his term of office, becomes an honorary president for life. Colonel Thomann is the first pharmacist to hold the highest office in the Congress and the congratulations of the pharmacists of the United States go to him, with best wishes for a successful administration.—E. F. K.

FEDERAL FOOD, DRUG AND COSMETIC ACT.

The Conferees appointed by the Senate and House to consider variations in H. R. 5762, have submitted a report and the report has been adopted by the Senate and the House. The bill is now before the President for action. In general, the Conference Report defers the effective date of certain provisions of the Federal Act from June 25, 1939, to January 1, 1940. The Secretary of Agriculture is also given the power to postpone certain provisions relating to labeling to July 1, 1940, if the public interest is protected and if owners of labels, containers, etc., might suffer severe loss.

SECTIONS

BOARD OF REVIEW OF PAPERS (SCIENTIFIC SECTION).—*Chairman*, F. E. Bibbins; H. M. Burlage, W. G. Crockett, E. V. Lynn, C. O. Lee, L. W. Rising, L. W. Rowe, Heber W. Youngken, Ralph E. Terry, Carl J. Klemme.

CHANGES IN ERGOT WITH VARIOUS MOISTURE CONTENTS UNDER DIFFERENT CONDITIONS OF STORAGE.*,[1]

BY B. V. CHRISTENSEN[2] AND J. A. REESE.[3]

The purpose of this investigation was to study the changes taking place in ergot of various moisture contents under different conditions of storage. The U. S. P. XI requires that Ergot be preserved under all conditions of storage and transportation in water-proof and air-tight containers. These requirements have been subjected to severe criticism by importers and manufacturers of ergot preparations (1).

REVIEW OF THE LITERATURE.

Paulizky (2) reported in 1787 that some thirty years previously powdered ergot had been introduced into pharmacies under the name *pulvis ad partum;* that it was administered by midwives and physicians effectively, but it lost its action on keeping. This is probably the first reference to the deterioration of ergot.

Hirschberg (3), 1871, recommended that ergot be carefully dried and preserved in well-sealed vessels. Ficinus (4), 1873, suggested that powdered ergot, if deprived of fat by ether, would keep much better. Gerrard (5), 1875, suggested preserving ergot, when dry, by bottling it and fixing a piece of lime, tied in muslin, to the interior of the stopper. Mourrut (6), 1877, recommended the mixing of freshly powdered ergot with 5 per cent of powdered benzoin.

Zschiesing and Bombelon (7), 1881, and Perrett (8), 1882, suggested defatting as a means of preservation. Alpen (9), 1888, reported that ergot should be dried in thin layers, the last portion of moisture removed by exposure over lime or sulfuric acid in a desiccator, and stored in corked yellow bottles.

Grünfeld (10), 1892, alleged a rapid loss of activity for ergot (tested on the cock). He concluded that samples lose all their activity within eight months of the harvest.

Zanon (11), 1893, sealed ergot in jars in which there were alternate layers of perfectly dry sand and ergot. Keller (12), 1894, stated that in a properly-packed pulverized ergot the alkaloid will keep undecomposed for at least a year.

Meulenhoff (13), 1900, severely criticised Grünfeld's experiments; experimented with more cocks than Grünfeld and found hardly any loss of activity after two years.

Dahlin (14), 1912, concluded that when properly kept the alkaloidal content of ergot does not diminish. Tate (15), 1921, thought there was likelihood of a small increase in activity when ergot is stored. Forst (16), 1926, found that a sample of powdered ergot had lost 55 per cent of the alkaloids in six months. Burn and Ellis (17) found samples of old ergot very active.

Thompson (18), 1930, reported two samples of ergot that deteriorated more in air-tight containers than in paper bags in a dry place.

Pedersen (19), (20) reported that defatted ergot was more stable than ergot. Corran and Rymill (21), 1935, presented data to indicate that powdered ergot, in any form, is comparatively stable over periods of time varying from seven to eighteen months.

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* Presented before the Scientific Section, A. PH. A., Minneapolis meeting, 1938.

[1] Abstract of a thesis presented to the Graduate Council, University of Florida in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

[2] Director, School of Pharmacy, University of Florida.

[3] Assistant Professor of Pharmacognosy, Medical College of Virginia.

Rowe (22), 1937, found three old samples of ergot stored under ordinary conditions still equal in activity to the U. S. P. XI standard of potency. The moisture contents ranged from 3.91 per cent to 4.94 per cent.

EXPERIMENTAL.

Material.[1]—Twelve lots of ergot (35 Kg.) were used in this investigation. Four of these lots, A, B, C and D, had been examined by Christensen and Welch (23). Six lots, 1, 2, 3, 4, 5 and 6 (19 Kg.), were obtained in 1936. Five of these lots were labeled Portuguese Ergot, and one lot, Spanish Ergot. Two lots, 7 and 8 (14 Kg.), were obtained in 1937, and were labeled Portuguese Ergot. The authors were informed by the importer that these lots were from large shipments consisting of several tons; and that the majority of the Portuguese Ergot was of Spanish origin.

Storage.—Each lot of ergot was thoroughly mixed before preparing samples for storage. Samples of ergot, weighing from 60 Gm. to 500 Gm., were stored in completely filled, air-tight, wide-mouthed bottles; completely and half-filled, air-tight Mason jars; completely and half-filled, not sealed, Mason jars; completely and half-filled wide-mouthed bottles stoppered with a pledget of cotton; wide-mouthed bottles stoppered loosely with a cork; ground, glass-stoppered bottles; and in paper bags. The samples were kept at constant temperatures at 21, 27, 32 and 38° C., and at room temperature, for periods of time varying from three months to six years. The moisture contents were varied from 3.2 per cent to 12.8 per cent.

The moisture contents were adjusted by spreading the ergot in thin layers in an oven at 38° C., and by placing in humid chambers at a temperature not exceeding 38° C.

ASSAY PROCEDURE.

The U. S. P. XI Cock's Comb method and a modification of the colorimetric method of the British Pharmacopœia and Addenda were used in this investigation. The colorimetric method follows:

Assay: Extract 15 Gm. of ergot in No. 60 powder by percolation with Purified Petroleum Benzin until the fat is completely removed. Dry the extracted drug at a temperature not exceeding 40° C., transfer to a stoppered flask, add 150 cc. anesthetic ether and set aside for 10 minutes. Add 0.6 Gm. light magnesium oxide diffused in 25 cc. of water and shake the mixture at intervals during thirty minutes; add 1.5 Gm. of powdered tragacanth, shake vigorously, set aside ten minutes and filter through cotton into a separatory funnel 100 cc. of the ethereal solution, representing 10 Gm. of the ergot being assayed. Shake with 4 successive 10-cc. portions of a 1 per cent w/v solution of tartaric acid in water. A fifth extraction with a 5-cc. portion of the acid should give no precipitate with Mayer's reagent. If a precipitate is formed, continue the extraction with 5-cc. portions until a negative test is obtained. Mix the aqueous liquids, transfer to a porcelain dish, remove the dissolved ether by gentle warming on a water-bath in a current of air and add sufficient water to produce 40 cc. or other suitable volume. Mix 1 cc. with 2 cc. of the Allport-Cocking reagent (24) and let stand thirty minutes. In the same manner, mix 1 cc. of 0.012 per cent solution of Ergotoxine Ethanesulfonate in 1 per cent w/v tartaric acid in water (1 cc. of this solution contains the equivalent of 0.0001 Gm. of anhydrous ergotoxine) with 2 cc. of the Allport-Cocking reagent, and let stand for the same length of time. Determine the ratio of the color intensities by comparing them in a suitable colorimeter. The color produced by 1 cc. of 0.012 per cent solution of Ergotoxine Ethanesulfonate is equivalent to that produced by 0.0001 Gm. of total alkaloids under identical conditions. The acid solution of the alkaloids should be suitably diluted so that the color, produced during the test, does not differ by more than 20 per cent from that produced in the solution of Ergotoxine Ethanesulfonate.

Time may be saved by preparing dilutions of the acid solution of the alkaloids by mixing 1 part with 1, 2, 3, 4 and 5 parts of water, and mixing 1 cc. of each of these with 2 cc. of the Allport-Cocking reagent.

Allport and Cocking (24) have insisted on the use of pure anesthetic ether, to avoid oxidation of the alkaloids.

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[1] Acknowledgment is made to the U. S. P. XI Revision Committee for furnishing the greater part of the ergot used in this investigation and the Ergotoxine Ethanesulfonate.

PART I.

REËXAMINATION OF OLD ERGOT.

Four lots of ergot, 2 Spanish and 2 Russian, which had been examined by Christensen and Welch (23) were reëxamined. These samples had been stored at room temperature in ground, glass-stoppered bottles for six years.

The moisture content of the samples had not been determined prior to storage. After storage the moisture content was determined using the U. S. P. XI Toluene method.

Fluidextracts of the drug had been examined by the U. S. P. X Cock's Comb method and by the Smith colorimetric method (25), using a standard Fluidextract of Ergot as a standard. The per cent of alkaloids in the drug itself had not been determined. The samples were reëxamined using the U. S. P. XI Cock's Comb method and the colorimetric method previously described. Ergotoxine Ethanesulfonate, supplied by the Committee of Revision of the U. S. P. XI, was used as a standard.

It is realized that the results given in Table I are not to be compared directly; the methods used before and after storage were different. The unstable fluidextract had been used for a standard before storage, and the alkaloids had been determined of a fluidextract prepared from the drug, and not of the drug itself. This was before the discovery of the alkaloids of ergot freely soluble in water and they probably had been removed. In addition, from data obtained in Part V of this investigation, it would appear that the fluidextract does not represent the alkaloidal content of the drug.

TABLE I.—ASSAY OF LOTS A, B, C AND D BEFORE AND AFTER STORAGE FOR SIX YEARS IN GROUND, GLASS-STOPPERED BOTTLES

Lot No.	Moisture after Storage Per Cent.	Assay, U. S. P. X before Storage Per Cent.	Assay, U. S. P. XI after Storage Per Cent.	Smith Assay of Fluidextract before Storage Alkaloid Per Cent.	Alkaloids after Storage (Colorimetric) Per Cent.
A	8.3	350	60	0.076	0.168
B	12.7	175	Less than 40	0.065	0.102
C	11.7	135	Less than 25	0.042	0.034
D	12.8	140	Less than 25	0.037	0.006

The physical appearance of lots B, C and D (those of the highest moisture contents) was much the same. The fracture of the ergot was flexible, and the color of the fracture was mostly yellow-brown. The color of the fracture of a few of the ergots was lavender. The appearance of the Spanish Ergot, lot A, was by far the best. About one-half had a short fracture, white to grayish white in color; the rest a flexible fracture of a yellow-brown color.

DISCUSSION.

The results of this part of the investigation seem to indicate that there is a relationship between physical condition and quality of the drug as measured by the colorimetric and U. S. P. XI Cock's Comb assay. This caused the authors to observe carefully the physical condition of all the ergot stored later. The results obtained later show far less correlation between physical condition and quality of the drug.

The results given in Table I show far more deterioration of ergot with moisture content from 11.7 to 12.8 per cent than of ergot with moisture content of 8.3 per cent. This deterioration was enough to cause the drug to be practically worthless. The relationship of moisture content and deterioration of the drug was carefully studied in succeeding portions of this work.

Part II.

CHANGES IN ERGOT WITH VARIOUS MOISTURE CONTENTS STORED IN AIR-TIGHT CONTAINERS AT DIFFERENT TEMPERATURES.

This part of the investigation was undertaken to ascertain the deterioration of ergot, if any, in air-tight containers with moisture content from 6.6 per cent to 12.6 per cent stored at 21, 27, 32 and 38° C., corresponding to 70, 80, 90 and 100° F. respectively. Some samples were also stored at room temperature.

EXAMINATION OF LOTS 1, 2, 3 AND 4.

Samples were prepared from lots 1, 2, 3 and 4 as given under storage in Part I. Thirty-two samples of 60 Gm. each were sealed (air-tight) in completely filled, wide-mouthed bottles and placed in uniform temperature control ovens. Six samples of 200 Gm. each were sealed (air-tight) in completely filled, wide-mouthed bottles and kept at room temperature and 38° C.

The moisture content was determined by the U. S. P. XI oven method; the average of two determinations was taken.

The per cent of alkaloids of each of the four lots was determined by the colorimetric method given in Part I. Lots 3 and 4 were also assayed by the U. S. P. XI Cock's Comb method.

The physical appearance of the samples was observed at the end of each week for ten weeks. No mold filament was present on any of the samples with moisture content below 8 per cent. Some of the samples with moisture content from 10.2 to 12.6 per cent had mold filament while others did not. Most of the samples had a thin grayish white coating which caused the ergot to appear as if it had been dusted lightly with a grayish white powder. From the results obtained later, when the containers were opened and the coating that was present examined under the microscope, the authors believe that a thin coating of mold was present on almost every sample during the later part of the observation period.

The four tables which follow summarize the physical condition of the four lots of ergot after storage for seventeen months.

TABLE II.—PHYSICAL CONDITION OF LOT 1 STORED IN AIR-TIGHT CONTAINERS FOR SEVENTEEN MONTHS.

Temperature ° C.	Moisture Per Cent.	Estimated Per Cent with Slight Mold.	Estimated Per Cent with Mold Filament.	Color of Fracture Estimated Per Cent White or Grayish White.	Color of Fracture Estimated Per Cent Yellow-Brown.
21	6.8	5	..	95	5
27	6.8	5	..	95	5
32	6.8	10	..	95	5
38	6.8	10	..	90	10
21	10.5	75	5	25	75
27	10.5	75	5	25	75
32	10.5	90	..	10	90
38	10.5	90	5	5	95

TABLE III.—PHYSICAL CONDITION OF LOT 2 STORED IN AIR-TIGHT CONTAINERS FOR SEVENTEEN MONTHS.

Temperature ° C.	Moisture Per Cent.	Estimated Per Cent with Slight Mold.	Estimated Per Cent with Mold Filament.	Color of Fracture Estimated Per Cent White or Grayish White.	Color of Fracture Estimated Per Cent Yellow-Brown.
21	7.4	2	..	95	5
27	7.4	2	..	95	5
32	7.4	5	..	90	10
38	7.4	5	..	90	10

21	10.5	50	25	10	90
27	10.5	50	25	10	90
32	10.5	90	..	5	95
38	10.5	65	10	10	90

TABLE IV.—PHYSICAL CONDITION OF LOT 3 STORED IN AIR-TIGHT CONTAINERS FOR SEVENTEEN MONTHS.

Temperature ° C.	Moisture Per Cent.	Estimated Per Cent with Slight Mold.	Estimated Per Cent with Mold Filament.	Color of Fracture Estimated Per Cent White or Grayish White.	Color of Fracture Estimated Per Cent Yellow-Brown.
21	6.6	..	..	100	...
27	6.6	..	..	95	5
32	6.6	5	..	90	10
38	6.6	10	..	95	5
21	12.6	50	..	...	100
27	12.6	75	..	...	100
32	12.6	80	..	...	100
38	12.6	50	..	...	100

TABLE V.—PHYSICAL CONDITION OF LOT 4 STORED IN AIR-TIGHT CONTAINERS FOR SEVENTEEN MONTHS.

Temperature ° C.	Moisture Per Cent.	Estimated Per Cent with Slight Mold.	Estimated Per Cent with Mold Filament.	Color of Fracture Estimated Per Cent White or Grayish White.	Color of Fracture Estimated Per Cent Yellow-Brown.
21	8	5	..	95	5
27	8	10	..	90	10
32	8	10	..	90	10
38	8	10	..	90	10
21	10.2	60	5	50	50
27	10.2	60	5	25	75
32	10.2	50	25	25	75
38	10.2	90	..	5	95

As a general rule, the higher the moisture content and the temperature the greater the tendency of the ergot to have a fracture of a yellow-brown color. The color of the fracture became darker as the moisture content and temperature increased, varying from a light yellow-brown to a dark yellow-brown. The fracture of the ergot, with a moisture content below 8 per cent, was short; of that above 8 per cent, slightly flexible.

The results of the assays before and after storage are given in the next five tables.

TABLE VI.—ASSAY OF LOT 1 BEFORE AND AFTER STORAGE FOR SEVENTEEN MONTHS IN AIR-TIGHT CONTAINERS.

Temperature* ° C.	Moisture Per Cent.	Alkaloids before Storage (Colorimetric) Per Cent.	Alkaloids after Storage (Colorimetric) Per Cent.	Loss of Alkaloids Per Cent.
21	6.8	0.202	0.196	3
27	6.8	0.202	0.193	4.5
32	6.8	0.202	0.189	6.4
38	6.8	0.202	0.143	29.2
21	10.5	0.194	0.178	8.2
27	10.5	0.194	0.173	10.8
32	10.5	0.194	0.164	15.5
38	10.5	0.194	0.154	20.6

* Corresponding to 70, 80, 90 and 100° F., respectively.

TABLE VII.—ASSAY OF LOT 2 BEFORE AND AFTER STORAGE FOR SEVENTEEN MONTHS IN AIR-TIGHT CONTAINERS.

Temperature ° C.	Moisture Per Cent.	Alkaloids before Storage (Colorimetric) Per Cent.	Alkaloids after Storage (Colorimetric) Per Cent.	Loss of Alkaloids Per Cent.
21	7.4	0.223	0.218	2.2
27	7.4	0.223	0.216	3.1
32	7.4	0.223	0.201	9.9
38	7.4	0.223	0.192	13.9
21	10.5	0.216	0.191	11.6
27	10.5	0.216	0.187	13.4
32	10.5	0.216	0.183	15.3
38	10.5	0.216	0.161	25.5

TABLE VIII.—ASSAY OF LOT 3 BEFORE AND AFTER STORAGE FOR SEVENTEEN MONTHS IN AIR-TIGHT CONTAINERS.

Temperature ° C.	Moisture Per Cent.	Alkaloids before Storage (Colorimetric) Per Cent.	Alkaloids after Storage (Colorimetric) Per Cent.	Loss of Alkaloids Per Cent.
21	6.6	0.210	0.208	1
27	6.6	0.210	0.20	4.8
32	6.6	0.210	0.177	15.7
38	6.6	0.210	0.190	9.5
21	12.6	0.196	0.162	17.3
27	12.6	0.196	0.166	15.3
32	12.6	0.196	0.145	26.0
38	12.6	0.196	0.144	26.5

TABLE IX.—ASSAY OF LOT 4 BEFORE AND AFTER STORAGE FOR SEVENTEEN MONTHS IN AIR-TIGHT CONTAINERS.

Temperature ° C.	Moisture Per Cent.	Alkaloids before Storage (Colorimetric) Per Cent.	Alkaloids after Storage (Colorimetric) Per Cent.	Loss of Alkaloids Per Cent.
21	8	0.221	0.213	3.6
27	8	0.221	0.204	7.7
32	8	0.221	0.186	15.8
38	8	0.221	0.179	19.0
21	10.2	0.216	0.192	11.1
27	10.2	0.216	0.190	12.0
32	10.2	0.216	0.173	19.9
38	10.2	0.216	0.168	22.2

TABLE X.—COLORIMETRIC AND U. S. P. XI ASSAYS OF ERGOT BEFORE AND AFTER STORAGE FOR SEVENTEEN MONTHS.

Lot No.	Temperature ° C.	Moisture Per Cent.	Alkaloids before Storage (Colorimetric) Per Cent.	Alkaloids after Storage (Colorimetric) Per Cent.	U. S. P. XI Assay before Storage Per Cent.	U. S. P. XI Assay after Storage Per Cent.
3	38	12.6	0.196	0.144	100	70
4	38	8.0	0.221	0.179	110	100
3	Room	6.6	0.210	0.20	100	100
4	Room	10.2	0.216	0.190	110	100
4	Room	8.0	0.221	0.205	110	110

A sample of lot 2, which was left in the original container for two years, was infested with bugs. The container was partially filled and air-tight. The sample still contained 0.18 per cent alkaloids.

A sample of lot 3, 12.6 per cent moisture, in a partially filled, loosely stoppered bottle at room temperature for fifteen months, was so molded that the ergot was almost beyond recognition. The sample had been in a moldy condition for more than a year. It contained 0.196 per cent alkaloids before storage; after storage, 0.106 per cent.

DISCUSSION.

The purpose of this investigation is not a study of assay methods; yet in order for the work to be of any value the methods of evaluation of the drug must be reliable. Examination of Table X shows that ergot assaying 100 to 110 per cent U. S. P. XI contained approximately 0.2 per cent total alkaloids. In order for a fluidextract of ergot to be U. S. P. XI it must contain active alkaloids corresponding to 0.05 per cent Ergotoxine Ethanesulfonate. Ergotoxine Ethanesulfonate contains 82 per cent ergotoxine. The fluidextract must then contain active alkaloids equivalent to 0.04 per cent anhydrous ergotoxine. Yet fluidextracts prepared from ergot assaying approximately 0.2 per cent alkaloids colorimetrically showed only 0.04 to 0.05 per cent alkaloid (as ergotoxine) by the U. S. P. XI Cock's Comb method. If the fluidextracts contained most of the alkaloids of ergot, then only 20 to 25 per cent of the alkaloids of ergot (as ergotoxine) were active in producing a bluing of the cock's comb.

Many investigators (26), (27), (28), (29), (30) have reported a fairly good agreement between the colorimetric and Cock's Comb assays of fluidextract of ergot. The Sub-Committee on ergot of the British Pharmacopœia (31) reached the conclusion that the results by the biological methods are lower than those obtained by chemical methods; the ratio of the average result is 2:1. Many workers have reported chemical assays of samples of ergot containing from 0.15 to 0.25 per cent alkaloids, but most of the chemical assays of fluidextracts of ergot reported are below 0.1 per cent. The authors reasoned from the preceding statements that the fluidextract does not represent the alkaloidal content of ergot and carried out experiments to find out if this is true.

Part V of this work tends to show that 40 to 65 per cent of the total alkaloids of ergot are as active in producing a bluing of the cock's comb as ergotoxine, and that the fluidextract contains approximately 50 per cent of the total alkaloids and approximately the same proportion of the ergonovine. With this in mind, Table X shows a fairly good agreement between the colorimetric and Cock's Comb assays.

Tables VI, VII, VIII, IX and X tend to show that ergot stored in air-tight containers with moisture content from 6.6 to 12.6 per cent deteriorates slowly. The deterioration with moisture content below 8 per cent at 21 and 27° C. was scarcely appreciable. Ergot with less than 8 per cent moisture at 32 and 38° C. deteriorated less than 16 per cent in all cases but one. No reason can be given to explain why one sample with 6.8 per cent moisture at 38° C. deteriorated more than the other samples at the same temperature. Ergot with moisture contents between 10.2 and 12.6 per cent deteriorated a maximum of 27 per cent as measured colorimetrically; a maximum of 30 per cent determined biologically. The amount of deterioration was generally proportional to the moisture content and the temperature.

From these five tables it can be seen that the deterioration of ergot in air-tight containers for seventeen months with moisture contents not greater than 12.6 per cent stored at 21, 27, 32 and 38° C. was usually too small to be measured biologically.

MOISTURE CONTENT OF ERGOT BEFORE AND AFTER STORAGE IN AIR-TIGHT CONTAINERS.

It has been inferred (1) that the moisture content of ergot stored in air-tight containers would increase as much as 3 per cent. In order to ascertain whether any such change would take place under the storage conditions employed in this investigation, the moisture content of a representative number of samples was redetermined. The difference in all cases was within the limit of experimental error. The results are given in Table XI.

TABLE XI.—MOISTURE CONTENT OF ERGOT BEFORE AND AFTER STORAGE IN AIR-TIGHT CONTAINERS.

Lot No.	Temperature ° C.	Period of Storage Months.	Moisture Content Before Storage.	Moisture Content After Storage.
2	21	17	7.4	7.6
2	27	17	7.4	7.6
2	32	17	7.4	7.5
2	38	17	7.4	7.5
1	21	17	10.5	11.0
1	27	17	10.5	10.6
1	32	17	10.5	11.0
1	38	17	10.5	10.5
6	27	7	10.2	10.1
6	32	7	10.2	10.3

PART III.

CHANGES IN ERGOT WITH VARIOUS MOISTURE CONTENTS STORED IN OPEN AND CLOSED CONTAINERS AT DIFFERENT TEMPERATURES.

This part of the investigation was undertaken to ascertain whether it is necessary to store ergot in air-tight containers. Ergot with moisture contents from 3.2 to 10.2 per cent was stored in open and closed containers at 21, 27, 32 and 38° C. and at room temperature.

EXAMINATION OF LOTS 5, 6, 7 AND 8.

Lots 5 and 6 were received in air-tight containers. These lots showed some sign of mold, and a very small quantity of the ergot was discarded. Lot 5 was in better condition than lot 6. Both lots were in fairly good condition, but, to prevent further mold before the ergot was stored, the two lots were spread in thin layers and exposed to the sun for three hours. After this treatment, lot 5 tested 9.2 per cent moisture; lot 6, 10.2 per cent.

Lots 7 and 8 were received in paper bags and were in excellent condition. Lot 7 had 9.2 per cent moisture; lot 8, 9.7 per cent.

The four lots were assayed by the colorimetric method given in Part I and by the U. S. P. XI Cock's Comb method.

Sixty-four samples were prepared and stored as given under storage in Part I. The weight of each sample was from 200 Gm. to 500 Gm.

The physical appearance of the samples of lots 5, 6, 7 and 8 was observed from time to time. The appearance as a rule was similar to lots 1, 2, 3 and 4. The samples with a moisture content greater than 7 per cent at 27, 32 and 38° C. in paper bags and loosely closed containers were in better condition than the samples at the same temperatures in air-tight containers. The difference in some cases was more marked than in others.

A sample of lot 7, stored in air-tight container at 27° C. with a moisture content of 9.6 per cent, had mold filament on more than half of the ergot, while another sample of the same moisture content and at the same temperature in loosely closed container had no mold filament and was in far better condition. The moisture content of the sample in loosely stoppered container decreased from 9.6 per cent to 8.5 per cent.

Some sign of mold was present in all the samples with a moisture content greater than 9 per cent regardless of the condition of storage. In some samples the mold was present as filaments readily recognizable, while in others only a thin grayish white coating was present on some of the ergots. No mold was present on any of the samples with a moisture content less than 6 per cent regardless of the storage condition.

The results before and after storage are given in Tables XII to VIII inclusive.

TABLE XII.—COLORIMETRIC AND U. S. P. XI ASSAY OF LOT 5 BEFORE AND AFTER STORAGE FOR SEVEN MONTHS IN HALF-FILLED, SEALED (AIR-TIGHT) CONTAINERS.

Temperature ° C.	Moisture Per Cent.	Alkaloids before Storage (Colorimetric) Per Cent.	Alkaloids after Storage (Colorimetric) Per Cent.	U. S. P. XI Assay before Storage Per Cent.	U. S. P. XI Assay after Storage Per Cent.
21	3.2	0.221	0.219	130	120
27	3.2	0.221	0.220	130	110
32	3.2	0.221	0.218	130	120
38	3.2	0.221	0.214	130	110
21	9.2	0.207	0.191	130	110
27	9.2	0.207	0.187	130	110
32	9.2	0.207	0.180	130	100
38	9.2	0.207	0.195	130	110

TABLE XIII.—COLORIMETRIC AND U. S. P. XI ASSAYS OF LOT 5 BEFORE AND AFTER STORAGE FOR SEVEN MONTHS IN LOOSELY-CLOSED MASON JARS.

Temperature ° C.	Moisture before Storage Per Cent.	Moisture after Storage Per Cent.	Alkaloids before Storage (Colorimetric) Per Cent.	Alkaloids after Storage (Colorimetric) Per Cent.	U. S. P. XI Assay before Storage Per Cent.	U. S. P. XI Assay after Storage Per Cent.
21	3.2	3.6	0.221	0.218	130	110
27	3.2	3.2	0.221	0.219	130	120
32	3.2	3.1	0.221	0.217	130	110
38	3.2	3.1	0.221	0.215	130	110
Room	3.2	4.3	0.221	0.218	130	120
21	9.2	8.9	0.207	0.197	130	100
27	9.2	8.1	0.207	0.199	130	110
32	9.2	7.8	0.207	0.196	130	120
38	9.2	6.9	0.207	0.193	130	100
Room	9.2	9.2	0.207	0.187	130	100

TABLE XIV.—COLORIMETRIC AND U. S. P. XI ASSAYS OF LOT 6 BEFORE AND AFTER STORAGE IN FILLED, SEALED (AIR-TIGHT) CONTAINERS FOR SEVEN MONTHS.

Temperature ° C.	Moisture Per Cent.	Alkaloids before Storage (Colorimetric) Per Cent.	Alkaloids after storage (Colorimetric) Per Cent.	U. S. P. XI Assay before Storage Per Cent.	U. S. P. XI Assay after Storage Per Cent.
21	3.7	0.206	0.208	120	120
27	3.7	0.206	0.204	120	...
32	3.7	0.206	0.202	120	...
38	3.7	0.206	0.201	120	110
21	10.2	0.192	0.177	120	100
27	10.2	0.192	0.181	120	...
32	10.2	0.192	0.179	120	...
38	10.2	0.192	0.179	120	100

TABLE XV.—COLORIMETRIC AND U. S. P. XI ASSAYS OF LOT 6 BEFORE AND AFTER STORAGE FOR EIGHT MONTHS IN PAPER BAGS.

Temperature ° C.	Moisture before Storage Per Cent.	Moisture after Storage Per Cent.	Alkaloids before Storage (Colorimetric) Per Cent.	Alkaloids after Storage (Colorimetric) Per Cent.	U. S. P. XI Assay before Storage Per Cent.	U. S. P. XI Assay after Storage Per Cent.
21	3.7	3.8	0.206	0.204	120	120
27	3.7	..	0.206	0.209	120	...
32	3.7	..	0.206	0.204	120	...
38	3.7	..	0.206	0.203	120	110
Room	3.7	4.3	0.206	0.207	120	130
21	10.2	9.6	0.192	0.181	120	120
27	10.2	..	0.192	0.182	120	...
32	10.2	..	0.192	0.184	120	...
38	10.2	5.6	0.192	0.186	120	100
Room	10.2	10.1	0.192	0.180	120	110

TABLE XVI.—COLORIMETRIC AND U. S. P. XI ASSAYS OF LOT 7 BEFORE AND AFTER STORAGE FOR FOUR MONTHS IN FILLED, SEALED (AIR-TIGHT) CONTAINERS.

Temperature ° C.	Moisture Per Cent.	Alkaloids before Storage (Colorimetric) Per Cent.	Alkaloids after Storage (Colorimetric) Per Cent.	U. S. P. XI Assay before Storage Per Cent.	U. S. P. XI Assay after Storage Per Cent.
21	6.7	0.230	0.231	110	110
27	6.7	0.230	0.229	110	...
32	6.7	0.230	0.227	110	...
38	6.7	0.230	0.224	110	110
Room	6.7	0.230	0.228	110	120
21	9.6	0.223	0.216	110	100
27	9.6	0.223	0.203	110	...
32	9.2	0.224	0.216	110	...
38	9.2	0.224	0.212	110	110

TABLE XVII.—COLORIMETRIC AND U. S. P. XI ASSAYS OF LOT 7 BEFORE AND AFTER STORAGE FOR FOUR MONTHS IN LOOSELY-STOPPERED CONTAINERS.

Temperature ° C.	Moisture before Storage Per Cent.	Moisture after Storage Per Cent.	Alkaloids before Storage (Colorimetric) Per Cent.	Alkaloids after Storage (Colorimetric) Per Cent.	U. S. P. XI Assay before Storage Per Cent.	U. S. P. XI Assay after Storage Per Cent.
21	6.7	...	0.230	0.229	110	120
27	6.7	...	0.230	0.225	110	...
32	6.7	...	0.230	0.227	110	...
38	6.7	...	0.230	0.228	110	110
21	9.6	...	0.223	0.217	110	100
27	9.6	8.5	0.223	0.218	110	...
32	9.2	7.2	0.224	0.220	110	...
38	9.2	...	0.224	0.223	110	110

TABLE XVIII.—COLORIMETRIC AND U. S. P. XI ASSAYS OF LOT 8 BEFORE AND AFTER STORAGE FOR FIVE MONTHS IN FILLED, SEALED (AIR-TIGHT) CONTAINERS.

Temperature ° C.	Moisture Per Cent.	Alkaloids before Storage (Colorimetric) Per Cent.	Alkaloids after Storage (Colorimetric) Per Cent.	U. S. P. XI Assay before Storage Per Cent.	U. S. P. XI Assay after Storage Per Cent.
21	6.3	0.217	0.220	120	130
27	6.3	0.217	0.214	120	...
32	6.3	0.217	0.218	120	...
38	6.3	0.217	0.206	120	120
Room	6.3	0.217	0.217	120	...
21	9.7	0.209	0.203	120	100
27	9.7	0.209	0.205	120	...
32	9.7	0.209	0.20	120	...
38	9.7	0.209	0.195	120	...
Room	9.7	0.209	0.192	120	110

DISCUSSION.

The results recorded in the preceding tables tend to show that the deterioration of ergot with moisture content from 3.2 to 10.2 per cent stored in open and closed containers at 21, 27, 32 and 38° C. is very slight. The amount of deterioration was too small to be measured biologically. The differences in the results obtained by the U. S. P. XI Cock's Comb assay are within the limits of experimental error.

The deterioration of the alkaloids, determined colorimetrically, of the samples containing less than 7 per cent moisture, stored at 21, 27, 32 and 38° C. and at room temperature was negligible, regardless of the type of container used.

There was a slight deterioration of the alkaloids, determined colorimetrically, in the samples containing from 9.2 to 10.2 per cent moisture. The maximum deterioration of any sample was 13 per cent. The deterioration was generally proportional to the moisture content and the temperature.

This work tends to show that it is not necessary to store ergot in air-tight containers. At 27, 32 and 38° C., with moisture contents greater than 9 per cent, there was slightly less deterioration in loosely stoppered containers and paper bags than in air-tight containers. Since the moisture content of the samples in loosely stoppered containers and paper bags decreased, this probably explains why they deteriorated less than the samples in air-tight containers.

PART IV.

RELATIONSHIP OF ERGONOVINE TO THE TOTAL ALKALOIDS OF ERGOT AFTER STORAGE OF THE DRUG WITH VARIOUS MOISTURE CONTENTS AT DIFFERENT TEMPERATURES.

This part of the investigation resulted from the thought that possibly ergonovine may deteriorate faster than the other alkaloids of ergot. If this is true, neither the colorimetric determination of the total alkaloids nor the U. S. P. XI Cock's Comb assay will give any indication of this deterioration.

Unfortunately, the authors knew of no satisfactory method for the determination of ergonovine prior to storage. Since the deterioration of the samples of ergot at 21° C. containing less than 8 per cent moisture was almost negligible, it is hoped that the results are significant. Since the isolation of ergonovine (32), (33), (34), (35), (36), (37), (38), considerable interest has been manifested in this alkaloid, and it has been said that it is "the true active principle of ergot" (39). An isomer of this alkaloid has been reported by Smith and Timmis (40).

Trabucchi (41) reported a method for the determination of ergonovine in ergot preparations based on the principle that ergonovine is precipitated with picric acid only in strong concentrations, while the other alkaloids are precipitated completely in weak concentrations. This method was utilized in this work.

The tartaric acid solution of the alkaloids obtained in the colorimetric method described in Part I was treated with a saturated aqueous solution of picric acid (approximately 10 per cent of its volume) and filtered. The ergonovine was determined in the filtrate by the colorimetric method. Usually 1 cc. of the picric acid solution was added to 10 cc. of the alkaloidal solution; the precipitated alkaloids filtered off; 1 cc. of the filtrate mixed with 2 cc. of the Allport-Cocking reagent, and the color compared in a suitable colorimeter as described under the colorimetric method. If the color produced differed by more than 20 per cent from the standard, suitable dilutions were made of the Ergotoxine Ethanesulfonate solution. It was not found necessary to dilute the ergonovine solution. The ergonovine was calculated as anhydrous ergotoxine.

Samples from 6 of the lots of ergot, 1, 2, 3, 4, 5 and 6, were examined. The results are given in Table XIX.

TABLE XIX.—RELATIONSHIP OF ERGONOVINE TO THE TOTAL ALKALOIDS OF ERGOT AFTER STORAGE OF THE DRUG WITH VARIOUS MOISTURE CONTENTS AT DIFFERENT TEMPERATURES.

Lot No.	Temperature ° C.	Moisture Per Cent.	Period of Storage Months.	Total Alkaloids after Storage (Colorimetric) Per Cent.	Ergonovine (as Ergotoxine) after Storage (Colorimetric) Per Cent.	Ergonovine Per Cent of Total Alkaloids.
1	21	6.8	17	0.196	0.031	16
1	32	6.8	17	0.189	0.033	17
1	38	6.8	17	0.143	0.033	23
2	27	10.5	17	0.187	0.034	18
2	32	10.5	17	0.183	0.029	15
2	38	10.5	17	0.161	0.020	12
3	21	6.6	17	0.208	0.037	18
3	27	6.6	17	0.20	0.033	17
3	32	6.6	17	0.177	0.029	16
3	38	6.6	17	0.190	0.030	16
3	21	12.6	17	0.162	0.030	19
3	27	12.6	17	0.166	0.031	19
3	32	12.6	17	0.145	0.022	15
3	38	12.6	17	0.144	0.015	10
4	21	8.0	17	0.213	0.037	17
4	27	8.0	17	0.204	0.033	16
4	32	8.0	17	0.186	0.033	18
4	21	10.2	17	0.192	0.035	18
4	27	10.2	17	0.190	0.033	17
4	32	10.2	17	0.173	0.028	16
5	27	9.2	7	0.187	0.033	18
5	32	9.2	7	0.180	0.032	18
6	27	10.2	7	0.181	0.035	19
6	32	10.2	7	0.179	0.034	19

DISCUSSION.

The relationship of ergonovine to the total alkaloids remained remarkably constant, averaging 17 per cent of the total alkaloids (both calculated as ergotoxine). Only 3 samples deviated any appreciable amount from the average. These were the following: (1) a sample from lot 1, moisture content 6.7 per cent at 38° C., ergonovine 23 per cent of total; (2) a sample from lot 2, moisture content 10.5 at 38° C., ergonovine 12 per cent of total; (3) a sample from lot 3, moisture content 12.6 per cent at 38° C., ergonovine 10 per cent of total.

With the possible exception of two of the samples at 38° C. these results give no indication that ergonovine deteriorates any faster than the other alkaloids of ergot.

PART V.

RELATIONSHIP OF THE ALKALOIDS OF ERGOT TO THE COCK'S COMB ASSAY.

This part of the investigation resulted from apparent discrepancies between the colorimetric and Cock's Comb assays of ergot. This work was done in order to determine if there is any correlation between the two methods. There was also some doubt concerning the reliability of the U. S. P. XI method in determining the deterioration of ergot.

Many investigators (26), (27), (28), (29), (30) have reported a fairly good agreement between the colorimetric and the Cock's Comb assay of Fluidextract of Ergot. The Sub-Committee

on ergot of the British Pharmacopœia (31) reached the conclusion that the results by the biological method are lower than those obtained by chemical methods; the ratio of the average result is 2:1.

The authors observed during the early part of this investigation that samples of ergot which had around 0.2 per cent total alkaloids by the colorimetric method assayed only 100 to 130 per cent U. S. P. when a fluidextract was prepared according to the U. S. P. XI procedure. In order for a fluidextract of ergot to be U. S. P. XI it must contain active alkaloids corresponding to 0.05 per cent Ergotoxine Ethanesulfonate. Ergotoxine Ethanesulfonate contains 82 per cent ergotoxine. The fluidextract must then contain active alkaloids equivalent to 0.04 per cent anhydrous ergotoxine. Yet fluidextracts prepared from ergot assaying approximately 0.2 per cent colorimetrically showed only 0.04 to 0.06 per cent alkaloid (as ergotoxine) by the U. S. P. XI Cock's Comb method. If the fluidextracts contained most of the alkaloids of ergot, then only 20 to 35 per cent of the alkaloids of ergot (as ergotoxine) were active in producing a bluing of the cock's comb. Many investigators have reported chemical assays of samples of ergot containing from 0.15 to 0.25 per cent of alkaloids, but most of the chemical assays of fluidextract of ergot reported are below 0.1 per cent. The authors reasoned that the fluidextract does not represent the alkaloidal content of ergot, and experiments were performed to find out if this is true.

The total alkaloids were extracted from 4 fluidextracts, two prepared from samples from lot 5 and two prepared from samples from lot 6. The following process was used:

Five cubic centimeters of the fluidextract are diluted with 25 cc. of distilled water, rendered slightly alkaline with 3 per cent ammonia water and extracted with successive portions of 50, 35, 30 and 25 cc. of ether. The ethereal solution is extracted with 5 successive portions of 5 cc. each of a 1 per cent w/v solution of tartaric acid in water. A sixth extraction with a 4 cc. portion of the acid should give no precipitate with Mayer's reagent. Mix the aqueous liquids, transfer to a porcelain dish, remove the ether by gentle warming on a water-bath in a current of air and add sufficient water to produce 25 cc. or other suitable volume. The total alkaloids and the ergonovine content are then determined as described in Part I and Part IV.

The results obtained from the four fluidextracts are given in Table XX.

TABLE XX.—COMPARISON OF THE TOTAL ALKALOIDS OF ERGOT, TOTAL ALKALOIDS OF FLUIDEXTRACT OF ERGOT, ERGONOVINE CONTENT OF ERGOT AND ERGONOVINE CONTENT OF FLUIDEXTRACT OF ERGOT.

Lot No.	Total Alkaloids of Drug (Colorimetric) Per Cent.	Total Alkaloids of Fluidextract (Colorimetric) Per Cent.	Ergonovine (as Ergotoxine) from Drug (Colorimetric) Per Cent.	Ergonovine (as Ergotoxine) from Fluidextract (Colorimetric) Per Cent.	U. S. P. XI Assay of Fluidextract.
5	0.187	0.091	0.033	0.017	110
5	0.180	0.087	0.032	0.015	100
6	0.181	0.105	0.035	0.016	110
6	0.179	0.10	0.034	0.018	100

The results given in Table XX show that the fluidextracts of ergot contained approximately half of the alkaloids of ergot and about half of the ergonovine. Yet these fluidextracts assayed 100 to 110 per cent U. S. P. XI.

Experiments were then performed in order to obtain some comparison between the total alkaloids of ergot (colorimetrically) and the action of these alkaloids on the cock's comb.

The total alkaloids were extracted by the procedure used in the colorimetric method described in Part I. The tartaric acid solution of the total alkaloids was adjusted so that 1 cc. was equivalent to 0.5 mg. of ergotoxine as determined colorimetrically. When necessary the solution of the alkaloids was evaporated to suitable volume by gentle warming on a water-bath in a current of air.

Using cockerels standardized with a solution of Ergotoxine Ethanesulfonate containing 0.5 mg. per cc., the solutions of the total alkaloids were injected into these cocks and the potency of the total alkaloids determined.

The amount of Ergotoxine Ethanesulfonate necessary to produce a satisfactory bluing varied from 0.08 to 0.25 mg. per Kg. usually between 0.1 and 0.15 mg. per Kg. The quantity of total alkaloids necessary to produce the same effect as the standard was from 1.2 to 2 times the amount. These results were obtained from 6 lots of ergot using over 400 injections with 60 standardized

cockerels. These results tend to show that from 50 to 80 per cent of the total alkaloids of ergot are as active in producing a bluing of the cock's comb as Ergotoxine Ethanesulfonate. Therefore, 40 to 65 per cent of the total alkaloids are as active in producing a bluing of the cock's comb as ergotoxine.

The above results explain the difference between the colorimetric assay of the alkaloids of ergot and the U. S. P. XI assay of a fluidextract of ergot. When ergot was assayed by preparing a fluidextract and testing it on the cock's comb, the results were always less than half that obtained by assaying the total alkaloids of the drug by the same method. This is shown in Table XXI.

TABLE XXI.—RELATIONSHIP OF THE TOTAL ALKALOIDS TO THE COCK'S COMB ASSAY.

Average of Samples from Lot No.	Cock's Comb Assay of Total Alkaloids (Extracted from Drug) in Terms of U. S. P. XI Standard Per Cent.	Cock's Comb Assay of Fluidextract of Drug in Terms of U. S. P. XI Standard Per Cent.
3	210	100
4	240	110
5	300	130
6	300	120
7	250	110
8	260	120

The results of this part of the investigation tend to show that Fluidextract of Ergot prepared according to the U. S. P. XI procedure does not represent the alkaloidal content of ergot. The U. S. P. XI procedure seems to extract about half of the total alkaloids and about half of the ergonovine. The activity of the fluidextract on the cock's comb was less than half the activity of the total alkaloids of the drug when measured in the same manner and in comparable dilutions.

SUMMARY.

Twelve lots of ergot (35 Kg.) were used in this investigation. Samples of ergot were stored in completely filled, air-tight containers; half-filled, air-tight containers; ground, glass-stoppered bottles; completely and half-filled, not sealed, containers; wide-mouthed containers, stoppered loosely with cork and with pledget of cotton; and in paper bags. The samples were kept at constant temperatures ranging from 21° C. to 38° C., and at room temperature, for periods of time varying from three months to six years. The moisture contents were varied from 3.2 per cent to 12.8 per cent.

The results obtained in Part I show that ergot with moisture contents above 11 per cent stored at room temperature in ground, glass-stoppered bottles, deteriorated considerably in six years. This deterioration was in some cases enough to cause the drug to be worthless. One sample with moisture content of 8.3 per cent stored under the same conditions and for the same length of time was still fairly active, indicating that moisture content plays an important part in the keeping qualities of ergot.

The results obtained in Part II show that ergot stored in air-tight containers at 21, 27, 32 and 38° C. for seventeen months, with moisture contents from 6.6 to 12.6 per cent, deteriorated slowly. The amount of deterioration was generally proportional to the moisture content and the temperature. The amount of deterioration of the drug with moisture contents below 8 per cent at 21° and 27° C. was scarcely appreciable. Ergot with less than 8 per cent moisture at 32 and 38° C. for seventeen months deteriorated less than 16 per cent in all but one case. Ergot with moisture contents between 10.2 and 12.6 per cent deteriorated a maximum of 27 per cent as measured colorimetrically; a maximum of 30 per cent determined biologically.

The change in physical condition of ergot with moisture contents greater than 8 per cent was much more pronounced than the amount of deterioration as measured by the colorimetric or Cock's Comb assays. The samples with moisture contents greater than 10 per cent possessed a fracture that was flexible and mostly yellow-brown in color. The quantity showing this type of fracture was proportional to the per cent of moisture and the temperature. The color of the fracture was darker as the moisture content and temperature increased. The samples of the same lot showing more physical change also showed more deterioration of the alkaloids; yet the physical change was pronounced (all of the ergot of some samples possessed a fracture of a yellow-brown color), while the maximum deterioration of any sample studied during the seventeen month period was 27 per cent of the alkaloids (colorimetric) and 30 per cent of the activity of the Cock's Comb assay.

Ergot stored at 21, 27, 32 and 38° C. in air-tight containers with moisture contents greater than 6.6 per cent may show some sign of mold. The mold is of little importance unless the moisture content is greater than 8 per cent; close examination is necessary in order to discover the mold. A thin coating of mold, which causes the ergot to appear as if it had been dusted lightly with a grayish white powder, may be present. Ergot with moisture contents greater than 8 per cent may or may not have mold filaments. A sample with a higher moisture content and less mold may lose more alkaloids than a sample with a lower moisture content with more mold, if these samples are stored under the same conditions. The presence of a slight amount of mold is more objectionable from an esthetic viewpoint than from the standpoint of the deterioration of the alkaloids.

The moisture content of ergot stored in air-tight containers did not change. The difference was always within the limit of experimental error.

The results obtained in Part III tend to show that the deterioration of ergot with moisture contents from 3.2 to 10.2 per cent stored in open and closed containers at 21, 27, 32 and 38° C. and at room temperature for seven months is very slight. The amount of deterioration was too small to be measured biologically. The deterioration of the alkaloids, determined colorimetrically, of the samples containing less than 7 per cent moisture was negligible, regardless of the type of container. There was a slight deterioration of the alkaloids, determined colorimetrically, in the samples containing from 9.2 to 10.2 per cent moisture. The maximum deterioration of any sample in eight months was 13 per cent. The deterioration was generally proportional to the moisture content and the temperature.

This part of the investigation tends to show that it is not necessary to store ergot in air-tight containers. At 27, 32 and 38° C. with moisture contents greater than 9 per cent, there was slightly less deterioration in loosely stoppered containers and paper bags than in air-tight containers. Since the moisture content of the samples in loosely stoppered containers and paper bags decreased, this probably explains why they deteriorated less than the samples in air-tight containers.

The physical appearance of the samples with moisture contents greater than 7 per cent at 27, 32 and 38° C. in paper bags and loosely closed containers was better than the samples at the same temperature in air-tight containers. The difference in some cases was more marked than in others. This probably was due to the decrease in moisture content of the samples.

Some sign of mold was present in all the samples with a moisture content greater than 9 per cent regardless of the condition of storage. In some samples the mold was present as filaments readily recognizable, while in others only a thin grayish white coating was present on some of the ergots. No mold was present on any of the samples with a moisture content less than 6 per cent regardless of the storage condition.

Part IV of this investigation indicates that, with the possible exception of samples at 38° C., the ergonovine in ergot does not deteriorate any faster than the other alkaloids of the drug. The relationship of ergonovine to the total alkaloids remained remarkably constant, the ergonovine content averaging 17 per cent of the total alkaloids (both calculated as ergotoxine).

The results obtained in Part V indicate that Fluidextract of Ergot prepared according to the U. S. P. XI procedure does not represent the alkaloidal content of the drug. The U. S. P. XI procedure seems to extract about half of the total alkaloids and about half of the ergonovine. The activity of the fluidextract on the cock's comb was less than half the activity of the total alkaloids of the drug when measured in the same manner and in comparable dilutions.

Results obtained from 6 lots of ergot using over 400 injections with 60 standardized cockerels indicate that from 50 to 80 per cent of the total alkaloids of ergot are as active in producing a bluing of the cock's comb as Ergotoxine Ethanesulfonate; 40 to 65 per cent as active as ergotoxine.

The results of the investigation show that the colorimetric method is far more satisfactory for determining the amount of deterioration of ergot than the Cock's Comb method.

CONCLUSIONS.

1. Moisture content is the most important factor in the deterioration of ergot.

2. The results of this investigation indicate that it is not necessary to store ergot in air-tight containers.

3. The amount of deterioration of ergot in seventeen months, with moisture content below 8 per cent, is almost negligible if kept below 27° C.

4. The amount of deterioration of ergot in seven months at 21, 27, 32 and 38° C., with moisture content below 6 per cent, is negligible regardless of the type of container.

5. Ergot with moisture content from 8 per cent to 12.8 per cent deteriorates slowly at 21, 27, 32 and 38° C. The amount of deterioration is generally proportional to the moisture content and the temperature.

6. The change in physical condition of ergot with moisture content greater than 8 per cent is much more pronounced than the amount of deterioration as measured by the colorimetric or Cock's Comb assays.

7. The moisture content of ergot in air-tight containers does not change.

8. The ergonovine in ergot does not deteriorate any faster than the other alkaloids of the drug at 21, 27 and 32° C.

9. The U. S. P. XI procedure for Fluidextract of Ergot seems to extract about half of the total alkaloids and about half of the ergonovine. This should be further investigated.

10. The activity of Fluidextract of Ergot on the cock's comb is less than half the activity of the total alkaloids of the drug when measured in the same manner and in comparable dilutions.

11. Fifty to eighty per cent of the total alkaloids of ergot are as active in producing a bluing of the cock's comb as Ergotoxine Ethanesulfonate; 40 to 65 per cent as active as ergotoxine.

12. The colorimetric method is far more satisfactory for measuring the deterioration of ergot than the Cock's Comb method.

13. If it is desirable to keep ergot for several years with a minimum of deterioration, it is recommended that the moisture content be reduced to around 4 per cent and then stored in air-tight containers or in a dry place. The moisture content may be reduced to around 4 per cent if the drug is spread in a thin layer in a drying oven at 38° C. for about twenty-four hours.

14. If the drug is to be used in about a year a moisture content below 8 per cent will permit only a slight deterioration. If stored in a dry place the moisture content will decrease and there probably will be no deterioration.

15. There probably will be more deterioration in ergot with moisture content above 8 per cent in air-tight containers than in open containers; hence, with moisture content above 8 per cent, open containers are recommended.

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PHENYL AND NAPHTHYL URETHANES AND THE CORRESPONDING DI-SUBSTITUTED UREAS.*

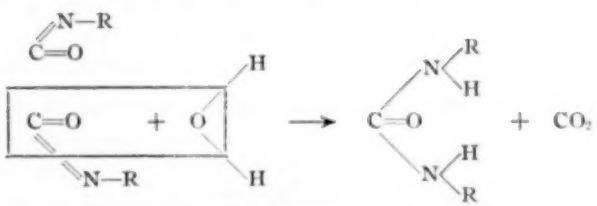
BY PAUL JANNKE.[1]

In a report on the study of *Gnaphalium obtusifolium* L., (1) it was stated that a phenyl urethane was prepared from a comparatively crude mixture of phenols. Though this derivative was easily prepared and readily separable from the reaction mixture, the naphthyl urethane of supposedly the same phenol was difficult to isolate from the unreacted substances and from di-α-naphthyl urea, a side reaction product.

Since the yield of di-α-naphthyl urea was so great when attempting to prepare the urethane of the unknown phenol, these questions arose:

(*a*) What precautions may be taken to prevent the formation of the di-substituted urea, and to assist the desired reaction? (*b*) What is the per cent of di-substituted urea contamination in the crystalline reaction product? (*c*) How might the urethane be separated from the di-substituted urea when the formation of the latter cannot be prevented?

It is a generally accepted fact that when an iso-cyanate comes into contact with moisture, the di-substituted urea is formed, and carbon dioxide is eliminated.



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* Presented before the Scientific Section, A. Ph. A., Minneapolis meeting, 1938.

[1] From the Laboratory of Edward Kremers.

It is for this reason that great care is taken to dry thoroughly the sample as well as the solvent (usually high boiling hydrocarbon). The hydrocarbon is used as a solvent with the assumption that the reaction product, the urethane, is poorly soluble in the hot hydrocarbon while the unreacted iso-cyanate and the side reaction product, the di-substituted urea, remain in solution. Numerous workers, however, have experienced the fact that α-β-diphenyl urea is but appreciably soluble in boiling kerosene and much less so in the cold solvent. Naturally, the di-α-naphthyl urea is far less soluble in both hot and cold kerosene.

Kamm (2) suggests the addition of an ethereal solution of trimethyl amine to catalyze the reaction, while other investigators have used aluminum chloride for the same purpose.

In his work on the phenyl and naphthyl urethanes of thymol, carvacrol and hydrothymoquinone, D. C. L. Sherk (3) does not report difficulty in obtaining pure products. He prepared these urethanes on a quantitative basis and reported the crystalline yields as being 100 per cent urethane. For example, the 71 per cent yield of thymol phenyl urethane was, according to its recorded melting point and nitrogen content, practically 100 per cent urethane, with little or no di-substituted urea present. As a further illustration, Sherk subjected 14 Gm. of crude hydrothymoquinone di-phenyl di-urethane to purification by extracting it once with boiling benzene, seven times with alcohol, three times with ethyl acetate and twice with acetone. None of these fractions does he regard as containing α-β-diphenyl urea, even though the melting point of the latter is but 4° higher than that of the di-urethane.

The urethanes of the three phenols, thymol, carvacrol and hydrothymoquinone, were prepared with strict adherence to the directions of Sherk, and with special attention given to the concentrated hydrocarbon mother liquors.

Urethane.	Percentage Yield. Sherk.	Jannke.	Melting Point. Sherk.	Jannke.	Mother Liquor Residue.
Thymol phenyl	71.0	70.3	106–7°	106–7°	Brown, sticky
Carvacrol phenyl	86.0	91.6	138°	136–7°	Brown, sticky
Hydrothymoquinone di-phenyl	83.2	60.0	229–30°	230–31°	Yellow, glass-like
Thymol α-naphthyl	43.0	76.4	156–7°	163–4°	Reddish brown, sticky
Carvacrol α-naphthyl	35.9	71.9	114°	104°	Reddish brown, sticky
Hydrothymoquinone di-α-naphthyl	67.8	..	...	135°	Brown
	93.8	..	135°	235°	Glass-like

Thus it becomes apparent that the crystals which Sherk separated from his various reaction mixtures were practically 100 per cent urethane, except in the case of the di-α-naphthyl urethane of hydrothymoquinone. In this he showed that a quantity of the mono-urethane was present along with some of the urea. For this same reason, the writer has not reported a figure for the percentage yield of that reaction, since the reaction product was definitely shown to be a mixture of 3 compounds whose identity was not established.

The observations made during the preparation of the phenyl urethanes of thymol and carvacrol were in agreement with those of Sherk. The hydrothymoquinone derivative, however, did not crystallize out of the cold hydrocarbon as Sherk reported, but instead, it separated as an insoluble body whose consistence depended upon the temperature; when warm, it was semi-solid, but when cold, it was brittle. When it was dissolved in boiling alcohol and the hot solution cooled, snow white, soft crystals of hydrothymoquinone di-phenyl di-urethane separated. The difference of 17 per cent in the total yield may be in part explained by the unusual way in which the derivative separated from the solution.

Sherk reported difficulty in causing the thymol α-naphthyl urethane to separate from its mother liquor. This, however, was contrary to the experience of the writer, in which case the entire reaction mixture set to a stiff mush as soon as it cooled a bit. So heavy was the deposit of urethane that no trace of solvent was visible until it was drawn off with suction. The mother liquid yielded no more crystals. The yield of the derivative was correspondingly higher than that reported by Sherk.

The observations on the carvacrol α-naphthyl urethane were not much different from those on the thymol derivative, except that it took about 10 hours for the reaction mixture to set to a mush. The dried crystals melted at 107°. When dissolved in alcohol and allowed to cool, a crop of crystals separated which melted at 288°, indicating that they were the di-substituted urea

When the mother liquor from them was concentrated and cooled, a large amount of crystals was obtained which melted at 104°. Recrystallization did not change the melting point. Evidently, the impurity raised the melting point of the urethane. In his experiments, Sherk did not observe di-α-naphthyl urea as an impurity in his carvacrol α-naphthyl urethane, and incidentally, the melting point of his pure urethane was 119°. Albers (4) recorded the melting point of this substance as 107°. Apparently, the α-naphthyl urethane is not a choice derivative for the identification of the phenol, for as Albers points out, only 3 of the 40 or more well-known workers on thymol and carvacrol problems have anything to say regarding the melting point of carvacrol α-naphthyl urethane. Even of these 3, one was shown to be working with the di-substituted urea instead of the urethane.

Identical with the case of the di-phenyl di-urethane of hydrothymoquinone and again opposite to Sherk's report, was the separation of the di-naphthyl di-urethane of hydrothymoquinone. Again, the derivative separated from the cooled hydrocarbon solution in the form of an insoluble liquid which solidified at a lower temperature. When recrystallized from alcohol, it melted at 232° with decomposition. Further recrystallization raised the melting point to 235° with but a trace of decomposition. This was insoluble in 1 per cent sodium hydroxide. The mother liquor (alcoholic) from these crystals yielded a second crop which, however, melted at 135°, and which dissolved in alkali with the production of a yellow color. A third crop of crystals was obtained, but this melted at 288°. In line with Sherk's reasoning, the compound melting at 135° may have been the mono-α-naphthyl urethane of hydrothymoquinone, as its solubility in alkali indicates the presence of a free hydroxyl group. The fact that the next compound is insoluble in alkali and melts at a higher temperature may show it to be the di-α-naphthyl urethane. The melting point of the third substance is indicative of its being di-α-naphthyl urea. If any analogy can be drawn from Kamm's (5) statement,[1] it is quite indefinite as to whether or not the di-urethane was present in the reaction product which seems to be a mixture of at least three substances.

On two occasions, Sherk mentions the melting point of di-α-naphthyl urea as 266–270°. This is not unusual, for an investigation on the literature showed that at least 5 different melting points are given for the same substance.

1879 Schiff (6), 270°; 1889 Vittenet (7), 314–315°; 1897 Pagliani (8), 270°, 1897 Clark and Young (9), 284–286°; 1920 Sherk (10), 266–270°; 1928 Clark (11), 314°; 1929 Beilstein (12), 289°.

The difference between melting points is caused not only by the methods of determining them, but also by the origin of the di-substituted urea. Thus, Schiff (13) points out that the ureas must not be heated long in determining their melting points, or, as in the case of the hydrazones and osazones, decomposition results. For this reason, when determining the melting point of the urea, the tubes with the samples were plunged into a bath previously heated to within a few degrees of the supposed melting point. It was repeatedly noted that when the temperature of the oil-bath was raised slowly, the sample of di-α-naphthyl urea melted enough to assume a wet appearance at 210°. At 260°, the sample became distinctly brown, and at 274–276°, it fused into a black liquid. However, when the test sample was plunged into a preheated oil-bath, it melted sharply at 289° with but a trace of decomposition.

Clark's reference for the high melting point of 314° is undoubtedly Vittenet who determined it by throwing the crystals onto a mercury-bath heated to that temperature.

When a few drops of α-naphthyl iso-cyanate were dissolved in boiling acetone, and water was added dropwise to produce cloudiness, the cooled reaction mixture yielded the di-substituted urea which melted at 288°. Recrystalization from benzene and from amyl acetate failed to change the melting point, but when some of the substance was sublimed under reduced pressure, the sublimate melted at 289°.

The melting point reported by Sherk for the di-substituted urea which he filtered from the iso-cyanate reagent was shown to be that of an impure compound. A quantity of it was dried during 2 weeks on a porous plate, in contact with air. Even at the end of this time, it smelled strongly of isocyanate, and appeared to be wet. That the urea was impure was shown by attempts to obtain duplicate melting points:

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[1] Kamm lists hydroquinone among the di-atomic phenols which do not react with α-naphthyl iso-cyanate.

264–265° with decomposition
249° with decomposition after softening at 230°
268° after softening at 230°
270° with decomposition.

When this substance was recrystallized from boiling amyl acetate, it melted at 288°. Recrystallization raised its melting point to 288.5°.

As was previously pointed out, the phenyl urethane was prepared of a crude, green mixture of phenols. Albers (14) was successful in preparing the phenyl urethanes of crude mixtures of thymol and of carvacrol obtained from various species of Monarda, when he utilized this reaction to conserve all of the small amounts of crude material. Thus, the urethanes may be used not only for identification purposes, but also for isolating phenolic substances, with a bit of consideration as to the nature of the crude material.

When applying the urethane reaction to a comparatively crude plant extract containing phenols, the temperature attained may often cause the liberation of moisture from some of the less stable compounds, in spite of the fact that the sample may have been thoroughly dried, with the subsequent formation of large amounts of di-substituted urea, thus contaminating the reaction product sometimes in excess of 50 per cent.

In preparing the α-naphthyl urethane of carvacrol, it was observed that the di-substituted urea crystallized out before any of the urethane did. In other cases, the urethane and the urea crystallized simultaneously. Hence the assumption that the urethanes are less soluble in high boiling hydrocarbons than the ureas are, and therefore crystallize out of the solution on cooling while the ureas remain dissolved, does not always hold true. Ethyl alcohol is an excellent solvent and crystallizing medium for the urethanes, but it is undesirable for separating mixtures of ureas and urethanes because with the excess of iso-cyanate present, some ethyl-alkyl urethane may form and add to the contamination.

As an unreacting solvent, ethylene dichloride was found highly desirable. The phenyl urethane of the unknown phenol from *G. obtusifolium* L., was exceedingly soluble in cold ethylene dichloride, while the α-β-di-phenyl urea was difficultly soluble even in the boiling solvent. Thus, an efficient separation of a mixture of these two substances was readily effected. In order to eliminate specificity and to allow for generalization, the solubility of the urethanes previously prepared was determined and is herewith compared. The solubility of each substance was determined at 22.5°, and is reported as the number of parts of solvent required to dissolve 1 part of substance.

Substance.	Solubility in: Alcohol.	Ethylene Dichloride.
Thymol phenyl urethane	4.96	2.40
Thymol α-naphthyl urethane	165.30	26.40
Carvacrol phenyl urethane	10.82	3.59
Carvacrol α-naphthyl urethane	18.70	9.20
Hydrothymoquinone di-phenyl di-urethane	405.70	512.00
Hydrothymoquinone di-α-naphthyl di-urethane	.....	.....
α β-Di-phenyl urea	135.30	681.60
Di-α-naphthyl urea	4516.00	2611.00

A study of the above table illustrates the practicability of ethylene dichloride treatment in separating the reaction mixture. For example, thymol phenyl urethane is approximately 300 times as soluble in ethylene dichloride (22.5° C.) as is α-β-di-phenyl urea, whereas in the case of alcohol being the solvent, the thymol phenyl urethane is only a bit more than 30 times as soluble as is the α-β-di-phenyl urea. It is true that di-α-naphthyl urea is about 1.7 times as soluble in ethylene dichloride as it is in alcohol, yet thymol α-naphthyl urethane is 100 times as soluble in ethylene dichloride as is di-α-naphthyl urea, while in alcoholic solution thymol α-naphthyl urethane is only 30 times as soluble as the di-substituted urea is. Ob-

viously, even in this extreme case the urethane can readily be separated from the di-substituted urea, using cold ethylene dichloride as the solvent.

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THE PREPARATION OF THE MANNONIC LACTONES FROM THE SEEDS OF THE DATE PALM (PHŒNIX DACTYLIFERA) AND A STUDY OF THEIR ACTION AND THAT OF NEW DERIVATIVES UPON GASTRIC MUCIN SMEARS.*,**

BY KARL J. GOLDNER[1] AND CHARLES H. ROGERS.[2]

The sugar lactones have been known for many years (1, 2), but it is only within comparatively recent times that they have assumed scientific and industrial importance.

From the viewpoint of theoretical organic chemistry, these compounds have been of great importance, since it was through them that the structure of the monosaccharides was proved. Also, the mechanism of the oxidation of the monosaccharides was not clearly understood until the properties of the lactones themselves had been determined.

The pharmaceutical uses of the sugar lactones include the substitution of gluconic acid for part of the citric acid in the preparation of Solution of Magnesium Citrate (3). It is said to produce a stable solution without the disagreeable sour taste of the pharmacopœial solution.

The calcium salts of the aldonic acids are used in calcium therapy and have been shown to be readily absorbed when administered orally (4). Calcium gluconate, included in the U. S. P. XI, has the advantage of being practically tasteless; non-irritant by hypodermic or intramuscular injection; and its intravenous toxicity is about a fourth that of calcium chloride (5).

In an investigation having for its purpose the determination of the relative merits of various dentifrices, Nichols, Hatton and Doherty (6) studied the effect of

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galactonic lactone on gastric mucin smears and found it to be superior to alkalis, soaps and most organic acids for the removal of mucin from glass slides. The removal of mucin from the teeth is important in preventive dentistry because fermentable food particles thoroughly mixed with salivary mucin and impacted between teeth or into pits and fissures against susceptible surfaces are, without doubt, an important factor in the formation of dental caries. As a result of this work, galactonic lactone has been incorporated into tooth pastes and mouth washes as a mucin solvent.

The source of galactonic lactone, which was the western larch, was being rapidly depleted, and a new source was sought. There appears at present to be no commercial utilization of the seeds of the date palm, of which large quantities are available from the preparation of seeded, sugared dates. These seeds have been reported by Tschirch (7), who states that they contain much hemicellulose which is composed of galactan and mannan and gives galactose and mannose on hydrolysis. Schulze, Steiger and Maxwell (8) report that the seeds, upon hydrolysis, liberate mannose and apparently also galactose.

Quantitative determinations of mannan and galactan were made in the laboratory. The seeds were found to contain 48.85 per cent of mannan and only 0.68 per cent of galactan. Obviously date seeds could not be used as a source of galactonic lactone. It was thought probable, however, that mannonic lactones and derivatives could be prepared and substituted for galactonic lactone as a mucin solvent.

The ethanolamines are organic bases of mild alkalinity and have been extensively used as emulsifying agents, to which use they are admirably suited. For these reasons it was thought that amides prepared from ethanolamines and mannonic lactone would be excellent substances for the removal of mucin since they would add the emulsifying properties of the ethanolamine to the lactone.

A few statements concerning the formation and behavior of lactones are given here to clarify the experimental work. The oxidation of sugars takes place through the oxide-ring structure with the direct formation of a lactone (9, 10, 11). Normal sugars yield first the δ-lactone (12, 13, 14). This δ-lactone is unstable in water and an equilibrium is rapidly established between the δ-lactone and the free acid. The free acid is then gradually converted to the γ-lactone, a reaction which has been shown to be irreversible at 20° (15).

EXPERIMENTAL.

Ash determinations on the ground seeds were made in the usual manner with the following average results:

Total ash—1.01 per cent

Water-insoluble ash—0.74 per cent

Water-soluble ash (by difference)—0.26 per cent

Alkalinity of water-soluble ash—0.26 cc. of 0.1*N* HCl were required to neutralize the water-soluble ash from one Gm. of seed.

Alkalinity of Water-Insoluble Ash.—1.04 cc. of 0.1*N* HCl were required to neutralize the water-insoluble ash from one Gm. of seed.

When extracted with petroleum benzine, date seeds yielded 8.4 per cent of a light yellow oil.

Quantitative Determination of Mannan (16).—Date seeds were hydrolyzed by boiling with dilute acid and the mannose formed precipitated as the phenyl hydrazone. The yield was equivalent to 54.23 per cent of mannose, or 48.85 per cent of mannan.

Quantitative Determination of Galactan (*17*).—The galactan of date seeds was oxidized by means of nitric acid to mucic acid, which was crystallized and weighed. The quantitity obtained was equivalent to 0.75 per cent of galactose, or 0.68 per cent of galactan.

Preparation of Mannose (*18*).—Mannose was prepared with a yield of 21.1 per cent of the date seeds used.

Preparation of Calcium Mannonate.—The method employed was similar to that of Isbell and Frush (19); however, instead of vegetable ivory, date seeds were used as the starting material. The only innovation was in the use of milk of lime and calcium carbonate to neutralize the acid used in hydrolysis. By this method, neutralization may be accomplished in less time than when calcium carbonate alone is used. Ninety-three grams of calcium mannonate were obtained from 300 Gm. of ground date seeds.

Some of the usual methods for inducing crystallization failed when applied to the solution of calcium mannonate. Concentration resulted in the formation of a gel. The addition of a small amount methanol, ethanol, dioxan or acetone produced colloidal precipitates. The addition of large amounts of methanol produced a hard mass, which, after innumerable washings and the expenditure of enormous quantities of methanol, was transformed to a white solid. This solid, however, could not be entirely freed from bromides, nor was it crystalline, and, therefore, could not be used for seed. Seed crystals were obtained from the National Bureau of Standards, and it was found that crystallization took place readily when the solution was seeded and not too concentrated.

Preparation of δ- and γ-Lactones.—A dry mixture of 40 Gm. of calcium mannonate and 10.6 Gm. of crystalline oxalic acid was added, with mechanical stirring, to 40 cc. of water. The resulting solution was filtered, an equal volume of dioxan added and the solution evaporated rapidly at 35° under reduced pressure. As the solution became more concentrated, δ-mannonic lactone crystallized, and three fractions were collected:

1. 5.8 Gm., melting at 163–165°
2. 4.8 Gm., melting at 159–161°
3. 3.4 Gm., melting at 159–161°.

A few drops of hydrochloric acid were added to the mother liquor and the solution evaporated to dryness. The crude lactone was recrystallized from water and gave 8 Gm. of pure γ-lactone, melting at 151°.

The specific rotation of the γ-lactone was found to be $[\alpha]_D^{20} = +51.00°$. This rotation did not change appreciably after several days at room temperature.

A solution of 0.4207 Gm. of the δ-lactone in 9.8933 Gm. of water gave the following rotations:

Time after Solution.	Rotation.	Specific Rotation.
4 min.	4.73°	114.2°
6 hr.	2.63°	63.5°
24 hr.	1.35°	32.6°
48 hr.	1.40°	33.8°
336 hr.	1.71°	41.3°

These results, which agreed approximately with those previously reported, indicated the establishment of an equilibrium between the δ-lactone and the free acid within 24 hours after solution. At this time there appeared to be about 28.5 per cent of δ-lactone and 71.5 per cent of free mannonic acid present in solution. The rotation was constant for several hours and then increased gradually until it approached that of the γ-lactone.

Derivatives of mannonic acid were prepared for the purpose of characterization and also with a view toward testing their action upon mucin smears. These derivatives were of three types: ethers, esters and amides.

The preparation of a phenyl ether was attempted. It was considered possible that sodium phenoxide would open the lactone ring, the phenyl group going to form a phenyl ether and the sodium going to form the sodium salt. Different attempts were made with benzene and with toluene as the solvent. An excess of sodium phenoxide was prepared, δ-gluconolactone was added, and the mixture refluxed. The product was precipitated as the calcium salt. The per cent of

calcium in this salt indicated that it contained at best about twenty per cent of the calcium salt of phenylgluconic acid.

Several esters of mannonic and gluconic acids were prepared by this procedure: The lactone was heated with the appropriate water-free alcohol, to which a drop of hydrochloric acid had been added. When the lactone was completely dissolved, the solution was filtered, concentrated and cooled to allow crystallization to take place.

Ethyl mannonate was prepared, melting at 161°. The specific rotation was zero, but this slowly increased until after two weeks it had become $[\alpha]_D^{20} = +31.9°$. From these results it was concluded that ethyl mannonate is optically inactive and that in aqueous solution it is slowly hydrolyzed. Because of the slowness of the hydrolysis the end-product, in addition to ethyl alcohol, is undoubtedly the γ-lactone.

Methyl mannonate was prepared, melting at 155°. The specific rotation was found to be $[\alpha]_D^{20} = +11.1°$. The rotation increased slowly until after 15 days it corresponded to $[\alpha]_D^{20} = +44.7°$.

Isopropyl mannonate was prepared, melting at 169°.

n-Butyl mannonate was also prepared, melting at 144°.

Esters of gluconic acid have much lower melting points than the corresponding esters of mannonic acid and become gummy at relatively low temperatures. They would be difficult to preserve in the solid state and, therefore, no further work was attempted with these substances.

To prepare the ethanolamide of mannonic acid, one Gm. of δ-mannonic lactone and 0.4 Gm. of ethanolamine were refluxed with 50 cc. of alcohol until solution was effected. The filtered solution was concentrated and cooled; whereupon crystallization took place immediately. A yield of 0.9 Gm. of a white, crystalline compound was obtained melting at 149–150°. The per cent of nitrogen, as determined by the Kjeldahl method, was found to be 5.76 per cent; calculated, 5.86 per cent. The specific rotation was found to be $[\alpha]_D^{20} = -14.4°$. In 48 hours, the rotation corresponded to $[\alpha]_D^{20} = -12.2°$. The amide may be concluded to be relatively stable in water.

The ethanolamide of gluconic acid was prepared similarly. Transparent, hard crystals were obtained, melting at 109°. The optical rotation was found to be $[\alpha]_D^{20} = +34.15°$. The rotation did not change after four days, showing that the amide is stable in aqueous solution at room temperature.

The diethanolamide of mannonic acid was prepared similarly. It was found, however, that from concentrated solutions the amide separated as a syrup, but that from dilute solutions a white amorphous solid gradually precipitated as the solvent evaporated spontaneously. This solid melted at 123°. The specific rotation of this amide was found to be $[\alpha]_D^{20} = +5.85°$.

The diethanolamide of gluconic acid was obtained only as a syrup. No amount of manipulation would give a solid compound.

TESTS ON MUCIN SMEARS.

Preparation of Mucin Smears.—One Gm. of Wilson's alcohol-washed mucin was placed in a beaker and to it added, with stirring, 15 cc. of a freshly prepared solution of sodium bicarbonate. The resulting mucinate, which had a p_H approximately that of saliva, was allowed to stand in the refrigerator until all air bubbles had been removed.

The films were made on ordinary microscope slides. The slides were first cleaned by soaking in cleansing solution (potassium dichromate-sulfuric acid), rinsed thoroughly with tap water then distilled water, placed in alcohol and dried with a towel. One-tenth of a cc. of the mucin mixture was measured with a graduated medicine dropper and spread on the slide over an area of 2″ by $^5/_8$″. The film was allowed to dry in air and a control slide made.

The mucin film was immersed in a saturated solution of mercuric bichloride for one minute. The slide was removed and washed with distilled water to remove the mercury salt and to determine whether the film adhered. The mercury bichloride fixed the mucin film firmly to the glass slide, and the film of the control slide was not removed when washed. The film was stained in a 0.5 per cent solution of malachite green. The film was washed with distilled water and allowed to dry.

In determining the effect of chemicals on the mucin film, the following method was used. The tooth brush, a Dr. Butler's single row tooth brush, was moistened with the solution of the chemical and stroked downward through the film three times, the pressure being the same a s i

used in the cleansing of the teeth. The slide was immediately placed in the solution of mercury bichloride to fix the film, and then washed with distilled water. The film was stained and photographed. The original method of Nichols, Hatton and Doherty was deviated from slightly in that the slides were washed before staining, since it was found that malachite green was precipitated by mercury bichloride.

The effect of alkaline substances was determined. When mucin smears were treated with a suspension containing equal quantities of milk of magnesia and water, the mucin was disturbed but not removed. A strong solution of Castile soap and five per cent sodium hydroxide solution gave similar results. The alkali appeared to make the mucin more viscous, and it adhered more tenaciously to the slide than it did before treatment. Lime water removed some of the mucin, although the effect was not appreciably greater than that of distilled water alone.

Acidic substances, on the other hand, removed mucin quite completely. A 0.5 per cent solution of citric acid removed mucin completely, while a 0.5 per cent solution of tartaric acid was only slightly less efficient.

The sugar lactones were next investigated, three per cent solutions being used. Of the γ-lactones, galactonic was better than either gluconic or mannonic. δ-Mannonic lactone removed nearly all of the mucin, and the equilibrium mixture of δ-lactone and free acid did remove all.

Derivatives of mannonic acid were also tested. Ethyl mannonate was not as efficient as the ethanolamide and diethanolamide

The results shown here are essentially the same as those obtained by the originators of the testing method. However, the conclusions arrived at by these workers are erroneous in that they apparently failed to take into consideration the reaction between the materials tested and the mercury bichloride. Alkaline and saponaceous substances react with mercury bichloride with the formation of the corresponding mercury salt. This mercury salt, being adhesive and insoluble in water, remains on the slide and is not removed in the regular process of washing. This film, when placed in the malachite green solution, takes up the stain, making the slide appear as though little or no mucin had been removed.

The apparent success of the acid solutions in removing mucin, as shown by this method, is explained by the fact that citric, tartaric, lactic and acetic acids and the lactones tested form soluble compounds with mercury, and these are removed from the slide by washing. Furthermore, the acid solutions prevent the mercury from fixing the mucin as mercury mucinate. Consequently, the mucin is almost entirely removed from the slide during the process of washing.

In order to determine whether the amides which had been prepared could safely be used in cleansing the teeth, toxicity tests were conducted. Rats were used as the test animals. The dose was calculated at four Gm. per Kg. of body weight and was injected intraperitoneally in ten per cent solution. Neither the ethanolamide nor the diethanolamide produced any ill effects, and it may be concluded that they are non-toxic.

SUMMARY.

1. The mannonic lactones have been prepared in good yield directly from date seeds, thereby establishing the possibility of date seeds as a commercial source of mannonic lactones.

2. Esters, ethanolamides and diethanolamides of gluconic and mannonic acids have been prepared and characterized.

3. The efficiency of mannonic lactones and amides as a solvent for mucin has been shown to be equal to that of galactonic lactone and organic acids, according to the method of Nichols, Hatton and Doherty.

4. It has been pointed out that, in the above method, alkaline and saponaceous substances react with mercury bichloride with the formation of insoluble, adhesive compounds; that acidic substances, including the lactones, form soluble mercury compounds; and that acidic substances prevent the fixing of mucin as mercury mucinate.

5. The ethanolamide and diethanolamide of gluconic acid have been shown to be non-toxic, even in massive doses.

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A STUDY OF ANTISEPTIC COMPOUNDS FOR THE TREATMENT OF BURNS.*,[1]

BY D. T. MEREDITH[2] AND C. O. LEE.[3]

INTRODUCTION.

The anesthetic properties of cocaine were noted in 1884, twenty-four years after the discovery of the alkaloid was announced (1). As a local anesthetic it has never been entirely acceptable because it often produces untoward effects. Since the determination of its structure many synthetic substitutes have been prepared and introduced into Medicine and Pharmacy.

The idea of reacting a local anesthetic with an antiseptic to form a new compound having both anesthetic and antiseptic action was first reported by Thayer (2) who prepared such a compound from butesin (normal-butyl-para aminobenzoate) and picric acid. His preparation represented a combination of one mole of picric acid and two moles of butesin and had the antiseptic and anesthetic properties of these respective compounds. Butesin picrate in the form of an ointment has been widely used in the treatment of burns.

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[1] An abstract of a thesis submitted to the faculty of Purdue University in partial fulfilment of the requirements for the degree of Master of Science, by Donald T. Meredith, August 1938.

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This study has been directed toward the preparation of a compound of the same type using benzocaine as the anesthetic. Such a product will be described later.

HISTORICAL.

Picric acid has long been known to have an antiseptic action and its phenol coefficient has been reported as 4 to 7. Its ability to form salts was the basis for Thayer's butesin picrate (2). Marshal (3) has given an interesting history of picric acid.

The value of picric acid as a treatment for burns was accidentally discovered by a French medical student about 1896 (4). Since then it has been used in the form of a saturated aqueous solution for this purpose.

There has been much conjecture as to the chemical nature and structure of complexes formed between polynitro-aromatic compounds, such as picric acid, and aromatic hydrocarbons and bases. Sudborough (5), (6) proposed several formulas to explain such reactions, concluding that they were additive and made possible by the latent valency in the trivalent nitrogen of the amines. He worked with α-naphthylamine and trinitrobenzene.

In discussing the probable structure of these complexes, Taylor and Baker (7) indicate that the point of attachment is the nitro group. Coghill and Sturtevant (8) suggest that such compounds do not represent a chemical union in the ordinary sense as the picric acid is joined to the second component by the so-called secondary valency forces such as are represented in the compound $CuSO_4.5H_2O$. Desha (9) suggests that double salts, such as the alums, furnished the best analogy to these complexes. From these and other authorities it is clear that there are many opinions and theories regarding the chemical nature of these complexes. Taylor and Baker concluded their discussion of the subject by saying that, "There is, however, insufficient evidence for any definite conclusion to be reached."

Benzocaine was introduced by Einhorne and Henry between 1897 and 1899, as a synthetic local anesthetic, to take the place of cocaine. It was named "anesthesine" in 1902 by Ritsert (11) and its anesthetic properties were described. The name "anesthesine" was changed to "benzocaine" in 1920 by the Council on Pharmacy and Chemistry of the American Medical Association (12). It was official in the United States Pharmacopœia X and has been retained in the present revision.

EXPERIMENTAL.

In undertaking the study it was our idea to try to prepare several anesthetic antiseptics but the work has been limited chiefly to the picrate of benzocaine.

Thayer (2) in 1925 indicated that the reaction of two moles of the local anesthetic with one mole of the picric acid yielded a compound in the combining ratio of 2:1. A year later (13) he directed that three moles of local anesthetic and one of picric acid would give a compound in the combining ratio of 3:1. He had previously reported an analysis (1) which indicated a compound of the 2:1 ratio. In his patent Thayer described benzocaine picrate as a solid with a melting point of 120° to 121°. Our results are not in agreement with his.

A picrate of benzocaine was first prepared following the procedure suggested for the preparation of butesin picrate, namely the reaction of one mole of picric acid, dissolved in water, with two moles of benzocaine, dissolved in alcohol. A yellow, amorphous precipitate resulted but it gave no definite melting point. In an effort to prepare a compound with a definite melting point, other solvents were used including those which had been suggested in the preparation of butesin picrate. The solvents used, melting points and descriptions of the compounds are given in Table I.

TABLE I.

	Solvents for Benzocaine.	Solvents for Picric Acid.	Product.	Melting Point (Uncorrected).
1	Alcohol	Water	Yellow, amorphous solid	Indefinite
2	Acidified water	Water	Yellow, crystalline solid	160–162°
3	Alcohol	Alcohol	Yellow, crystalline solid	160–162°
4	Ether	Ether	Yellow, crystalline solid	160–162°
5	Chloroform	Chloroform	Yellow, crystalline solid	160–160°
6	Benzol	Benzol	Yellow, crystalline solid	160–162°

Discussion.—Each of the six products in Table I was prepared in the same way, two moles of the benzocaine and one mole of the picric acid being dissolved separately in the respective solvents and the solutions mixed. The picric acid was dried over sulfuric acid before being used in the reaction.

In an effort to determine the difference between the first compound in Table I and the remaining five it was decided to analyze them for picric acid. This was done by titrating the picrate with tenth normal sodium hydroxide as suggested by Thayer (1). The results of the analyses of the compounds given in Table I are shown in Table II. The percentages of picric acid are averages of several titrations.

TABLE II.

	Solvents for Benzocaine.	Solvents for Picric Acid.	Melting Point (Uncorr.).	Per Cent Picric Acid.
1	Alcohol	Water	Indefinite	37.5%*
2	Acidified water	Water	160–162°	58.4%
3	Alcohol	Alcohol	160–162°	57.7%
4	Ether	Ether	160–162°	58.4%
5	Chloroform	Chloroform	160–162°	58.2%
6	Benzol	Benzol	160–162°	58.0%

* The percentages shown are the averages of two determinations.

Discussion.—From the results as shown in Table II, it is evident that compounds 2 to 6 are different from number 1, and they (2 to 6) are probably all alike. The calculated amounts for picric acid in picrates representing different combining ratios are as follows:

Benzocaine.	Picric Acid.	Ratio.	Calculated Per Cent Picric Acid.
3 moles	1 mole	3:1	31.62
2 moles	1 mole	2:1	40.96
1 mole	1 mole	1:1	58.11

A comparison of the calculated percentages of picric acid and the results obtained by analysis would suggest that benzocaine picrate is formed by one mole of benzocaine reacting with one mole of picric acid.

Several of the picrate compounds were assayed for benzocaine by making the solutions basic and extracting the latter by means of benzol, evaporating the solvent and weighing the benzocaine. Thayer (1) used ether as the solvent but it appeared to extract some of the picric acid. Since benzol did not extract any of the picric acid we preferred to use it as the solvent.

The calculated amount of benzocaine, in benzocaine picrate, is 41.90%. The yield of benzocaine by the assay just described was 41.30% in those compounds of the 1:1 ratio.

We were unable to prepare benzocaine picrate in the 3:1 or 2:1 ratios as suggested by Thayer. By purifying the compounds by means of recrystallization it was possible to get a product which would analyze as a compound of a 1:1 ratio. Furthermore, we were able to show that there was free benzocaine in compound 1, Tables I and II, while compounds 2 to 6 showed it to be absent.

THE PREPARATION OF BENZOCAINE PICRATE.

The following procedure for the preparation of benzocaine picrate is recommended:

Dissolve one mole of benzocaine in alcohol and one mole of picric acid in water. The latter may be warmed to facilitate solution. Mix the two solutions and allow to stand six to twelve hours. Filter off the precipitate, wash it with distilled water and dry it in the air.

The benzocaine picrate obtained by this procedure need not be recrystallized. It is a yellow, crystalline solid melting at 161–162° (uncorrected). The yield is 88% of the theoretical. The averages of several assays are as follows:

	Picric Acid.	Benzocaine.
Amounts calculated	58.10%	41.90%
Amounts obtained by assay	58.20%	41.30%

Following the method of Thayer butesin picrate was prepared which conformed to his descriptions for the product. We have no explanation for the difference in behavior exhibited by butesin and benzocaine in the formation of picrates.

BACTERIOLOGY AND PHARMACOLOGY.

Bacteriological and pharmacological tests were made on the various compounds which had been prepared. Two per cent ointments, in a special cold cream base, were prepared from benzocaine picrate 1:1; benzocaine picrate mixture, compound 1, Table I; and butesin picrate. None of these were antiseptic to Staphylococcus aureus when tested by the agar plate method. No further tests were made.

To test the anesthetic action of these various compounds the so-called "rabbit's eye" test was used, the procedure being similar to that employed by Rider (14). The results showed that all of the compounds studied have anesthetic action of like duration.

SUMMARY.

1. A picrate of benzocaine has been prepared which represents a compound of benzocaine and picric acid in the ratio of one mole of benzocaine to one mole of picric acid. This compound is a yellow, crystalline solid melting at 161–162° (uncorrected). Solvents and methods of preparation for this picrate are given, together with methods of determination of the amounts of benzocaine and picric acid.

2. This picrate differs from that one prepared by Thayer and covered by U. S. Patent 1,596,259, in the combining ratio of the benzocaine and picric acid. By analysis it is shown that the compound prepared in this investigation represents a compound in the ratio of one mole of benzocaine to one of picric acid. The compound has a melting point of 161–162°. The one described by Thayer in the patent mentioned above represents a combination in the ratio of three moles of benzocaine to one of picric acid and has a melting point of 120–121°.

3. All of the compounds studied; benzocaine picrate, the impure mixture of benzocaine picrate and benzocaine, and butesin picrate have an anesthetic action as indicated by the "rabbit's eye" test.

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FIELD TRIPS AUGMENT INTEREST IN PHARMACOGNOSY.*

BY VICTOR LEWITUS.[1]

(ABSTRACT.)

In order to increase interest in the course in Pharmacognosy, the writer thought it opportune to exhibit as many plants in their natural habitats as possible. He inaugurated a series of outdoor field trips, two during the fall of the year and two during the spring months.

Surprisingly enough, it was found worthwhile to use this method regularly as a part of the course since students introduced to this procedure were much more appreciative of the work in Pharmacognosy after a few introductory ramblings among the growing plants used in official medicine.

Remembering that a field trip is not a picnic (as the youthful student is apt to consider it), but a regular lesson for a serious, though enjoyable, portion of the day's study, careful plans must be laid by the instructor beforehand. Chronologically scheduled, the outdoor trips may be arranged so that two will come in the fall, when rhizomes, roots, barks and woods are usually treated of in the standardized courses; and two will occur in the spring, when flowers, leaves, etc., are taken up. The fall trip should come not earlier than the third or fourth lesson in the subject, since it will take that long to cover the introductory phases of the subject. Once acquainted with the purpose and procedure, the student is then ready to profit by his or her experiences.

The following rules should be a guide to those wishing to augment studies in Pharmacognosy by field trips:

I. The purpose of the trip should be clearly outlined a week or so beforehand.

II. Depending on the proximity of the area to be visited, the time devoted to such a trip should be arranged on an "exchange" basis with some other department (*e. g.*, exchange of hours).

III. Students should equip themselves with a special notebook; taking notes and making sketches as they go along.

IV. Notes should bring out the following details regarding each living drug: (*a*) Habitat (kind of soil, moisture, elevation); (*b*) Name of plant and synonyms;

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(*c*) Botanical family; (*d*) Part of plant official in medicine; (*e*) Brief historical sketch; (*f*) Reduced drawing showing representative portion of the whole living plant (in case it may be picked—see State Laws—draw the root or rhizome system also); (*g*) Drawing of the dried drug used in medicine (on return to the college).

V. Special credit may be assigned for students having the most carefully worked out field-trip notebook. All such books are returnable at the end of the course.

VI. Special reports on the plants encountered in the field, may be required by the instructor to improve habits of outside reading along the lines of the subject.

VII. The spot to be visited may be wooded land, field or even a botanical garden. It is best to visit virgin soil, a new spot to be selected during each of the trips. (The suggestive list of living drugs is too lengthy to include here.)

The results of such a series of field trips that may be expected are:

1. It associates for the student the name of the plant and its origin.
2. The student will better remember the part of the plant used in medicine.
3. Physical characteristics receive added emphasis.
4. Comparison before and after collection of the drug is afforded.
5. Presence of certain types of foreign matter are better understood.
6. The student is more apt to look into the historical background of a drug, since he is stimulated in this way.
7. This procedure builds up a better *cultural and scientific* background.
8. It enhances the general interest in the subject of Pharmacognosy.

FUNGAL INFESTATION OF POWDERED DRUGS.*

BY FANCHON HART.[1]

The eight drug powders susceptible to mold infestation selected for these experiments were: Althaea, Capsicum, Cascara, Ginger, Licorice, Rhubarb, Mustard and Sarsaparilla. All were sterilized, moistened with sterile water and inoculated with Aspergillus niger, Penicillium glaucum and Rhizopus nigricans. I noted the rate of growth and the abundance of each organism on the drugs used as culture media. Aspergillus and Rhizopus grew most rapidly and abundantly on Althaea; Penicillium most abundantly on Mustard and most rapidly on Licorice.

Fruiting stages were developed on most substances used. The portions of the powders exhibiting the spores showed no physical change but the vegetative forms of the fungus manifested definite changes in the starches of the various drugs. The iodine-starch test showed that changes occurred through vegetative growth. The starch in contact with the hyphae was rose-pink to bluish rose in comparison with the characteristic blue color.

On Althaea Rhizopus appeared as a buff-colored leathery mat with fine hairy surface dotted with the black sporangia. The leathery surface was stretched.

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* Presented before the Scientific Section, A. PH. A., Minneapolis meeting, 1938.

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The substrate remained exceedingly moist but the color of the powder was altered from the light yellow to chocolate-brown.

A fine grayish buff tangled mass of hyphae superimposed upon the drug characterized the infested cascara culture. Sporangia were not abundant but appeared along the edges.

The growth upon the powdered Ginger was raised above the drug and appeared as a cobwebby veil removed from the surface of the powder. Few fruiting bodies appeared on the meshes as well as near the edges.

Capsicum was completely covered with a thick tangled mass of hyphae interspersed with the dark sporangia. The appearance was that of a dark chocolate-brown hair felt. The undersurface of the growth was thin, tough and homogeneous in texture.

The growth on Licorice was about six millimeters thick. The texture was uniform throughout, presenting a loosely matted cover on and above the drug. The color shaded from dirty brown to dark gray on the edge.

Rhubarb developed a Rhizopus growth which appeared as spun glass over the surface without any gross manifestation of sporangia.

The Mustard plate was covered with a parchment-like structure similar to the vellum of agaric. A thin layer of matted hyphae with sporangia was attached to the surface.

The sporangia appeared most prominently on Sarsaparilla. The hyphae formed a scanty but closely knit cover over the drug. The fruiting bodies appeared as minute, dry, dark brown discrete pellets arising from the hyphal film.

Penicillia took the form of tiny cushions, punctate on the surface, with an occasional pilose covering of white hyphae when grown on Althaea. The powder was slightly darkened but the fungus was devoid of any color when examined with a simple lens.

Capsicum presented tiny crateriform convolutions with occasional darker regions in concave portions.

Beautiful formations occurred on Cascara. Tiny chocolate-brown furrowed rods completely covered the surface.

Ginger produced a yellow-brown powdery fungal growth of fruiting Penicillia with only a suggestion of the presence of a vegetative stage in the form of short fibers.

The appearance of the fungal plant on Licorice was similar in texture to the growth on Ginger but varied in that the sporangia imparted an olive-green color to the surface of the drug.

A cartilaginous covering of closely-matted hyphae, light tan in color and dotted with dark green sporangia, occurred on the powdered Rhubarb.

Mustard gave rise to a light green irregularly elevated surface covered with sporangia. Superimposed upon these was a creamy white tomentose layer of downy hyphae.

Dark bluish black mottled surface distinguished the growth of Penicillium on Sarsaparilla.

The rapidly growing spores of Aspergillus soon covered the surface of Althaea. A red-brown dry granular growth overshadowed the few fine vegetative threads.

Capsicum manifested a brownish red finely punctate surface as a result of the fungal culture. A yellowish buff layer supported the sporangia. This substratum was thick but brittle to the touch.

The purplish brown tiny globular masses of sporangia completely covered the hyphal surface growth on Cascara. The vegetative portion of Aspergillus on this drug formed a thin but tenacious pellicle.

The Ginger culture appeared as an irregularly lobed structure. The entire powder formed into a thick layer. The upper surface, with abundant sporangia, was dark reddish brown in color, having a granular texture. The undersurface of the culture was moist and sticky.

Small, regularly punctate spherical bodies of a reddish brown color characterize this growth on Licorice. The culture is only slightly moist.

On Rhubarb this fungus is light brown in color, small, yellowish papillose elevations appearing on the surface.

The alliaceous odor prominent on the Mustard culture of Aspergillus, differentiates this growth from the other cultures on Mustard as a medium. A small number of sporangia were present.

Sarsaparilla developed a dry, dark brown powdery mass of sporangia. No hyphae were apparent on this drug.

It is my belief that the medicinal substances and particularly drug powders may be utilized to differentiate the cultural characteristics of the fungi.

The possible change in structure and composition brought about through mold contamination is at present under investigation.

A HISTOLOGICAL STUDY OF HORSERADISH ROOT AND SOME COMMON ADULTERANTS.*

BY DR. CHARLES W. BALLARD[1] AND FRANK J. POKORNY.[1]

Horseradish Root (*Radicula Armoracia* L.) Rob. is a much-used condiment. Commercially, it occurs as the entire root, or it may be obtained in the grated and pickled condition. The authors recently had occasion to examine several samples of the grated root, purchased in the open market, and found that not all of the supposedly genuine roots were identical when seen under the compound microscope. Hence, a general study of the genuine Horseradish Root was initiated, along with certain other substances suspected as adulterants. These were the ordinary red beet, *Beta vulgaris* L.; turnip, *Brassica rapa* L.; and parsnip root, *Pastinaca sativa* L.

MORPHOLOGY OF HORSERADISH ROOT.

The genuine root occurs as a conical tap root, from one to two and a half feet in length, branched at the lower end; the roots sold commercially are usually one foot long and from one to two inches thick. The main root is cyclindraceous, tapers very slightly and is divided at the apex into three or more crowns, or stem bases, bearing annular leaf scars. The summit of each branch may bear a number of young leaves, pale green, or nearly white in color. Externally, the root is of light

* Presented before the Scientific Section, A. PH. A., Minneapolis meeting, 1938.

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yellowish brown color, and divides at its lower end into three or four vertical rows of fibrous secondary roots. Internally, the root is white and fleshy, the fracture is short and sharp; the transverse section shows a thin corky layer, and a thin, watery-looking line denotes the cambium, within which the xylem is indicated by a fine radiation. When broken or bruised, the root exhales a very pungent odor, and has a sharply biting acrid taste.

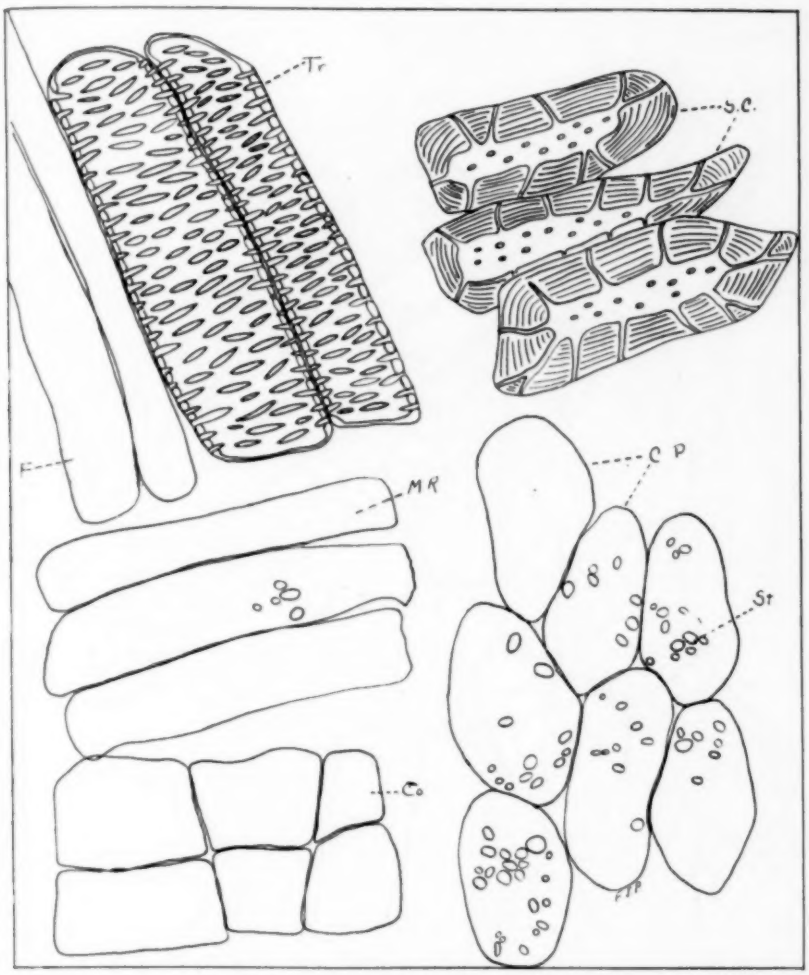

Fig. 1.—Horseradish Root (*Radicula Armoracia*). *C. P.*, cortical parenchyma; *F.*, fibers; *M. R.*, medullary ray cells; *St.*, starch; *S. C.*, stone cells; *Tr.*, reticulate tracheids. Camera lucida sketch (660 ×).

MICROSCOPY OF HORSERADISH ROOT.

Under the microscope, the cork consists of several layers of elongated, very thin-walled cells. These vary from 30 to 40 microns in width, 26 to 29 microns in length and 5 to 6 microns in thickness. Two to three layers of well-defined phelloderm cells are located under the cork. These cells are larger and slightly thicker-walled than the cork cells and are laid down in a very regular manner. The

cortical parenchyma consists of typical iso-diametric cells, measuring 48 microns in diameter. Large, isolated masses of stone cells occur in this region, the individual cells being thick-walled (8μ), pale amber in color, striated and porous. These cells vary in shape, from round to elongated rectangular, ranging in size from 58 microns long by 26 microns wide, to 107 microns long by 23 microns wide. These stone cells

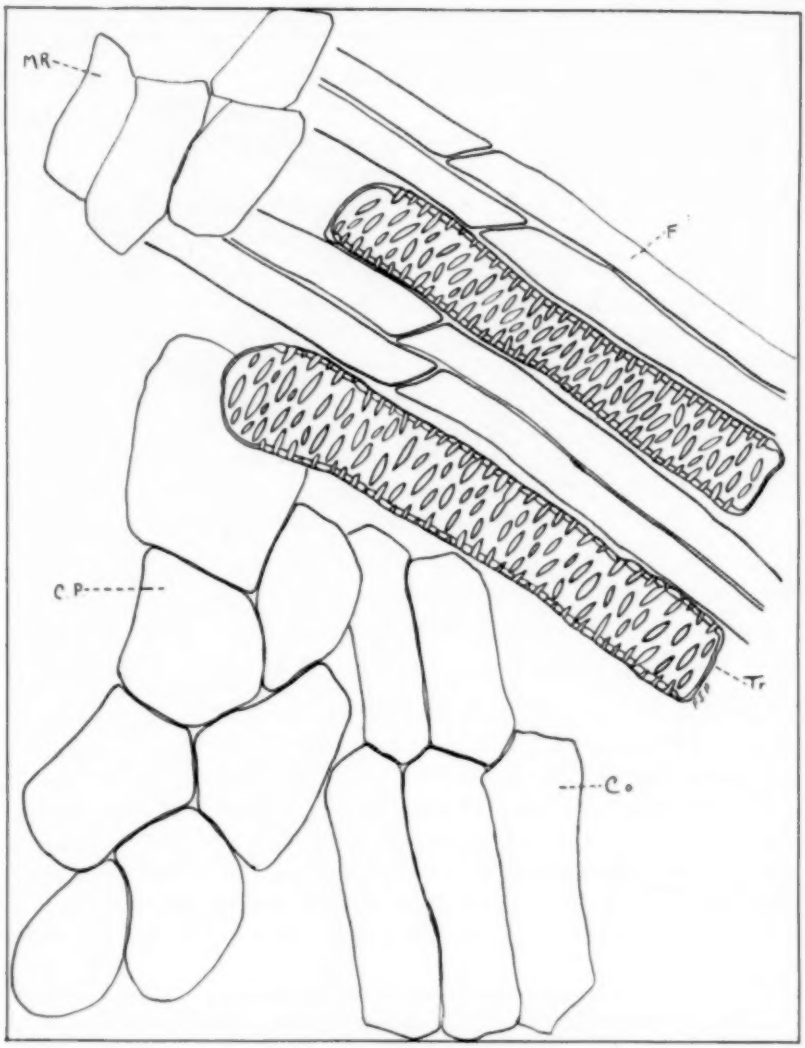

Fig. 2.—Beet Root (*Beta vulgaris*). *Co.*, cork; *F.*, fibers; *C. P.*, cortical parenchyma; *M. R.*, medullary ray cells; *Tr.*, reticulate tracheids. Camera lucida sketch (660 ×).

are very characteristic and could well serve as a diagnostic element. The pholem and cambium are very obscure in the grated product; medullary rays extend throughout the central region in a very regular and finely radiate arrangement. The ray cells average 26 microns in length, 98 microns in width and 26 microns wide in sectional view. In the grated condition bands of ray cells appear in long

fragments, and two or three cells in width. The inter-radial parenchyma cells are somewhat smaller than those of the cortex; otherwise, they show the typical isodiametric structure. Bast fibers are quite numerous in the cortex and occur as groups, the individual cells averaging 107 microns in length and 20 microns in width. The tracheids are very numerous and occur in groups of one to five or more, surrounded by the inter-radical parenchyma and the thin-walled elongated wood

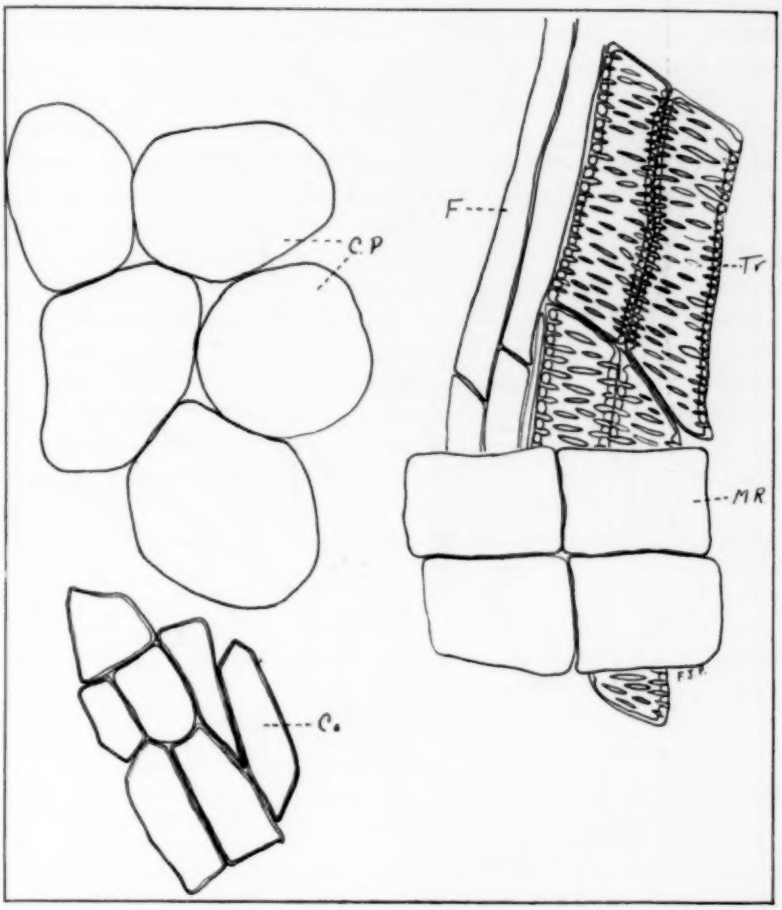

Fig. 3.—Turnip Root (*Brassica rapa*). *Co.*, cork; *C. P.*, cortical parenchyma; *F.*, fibers; *M. R.*, medullary ray cells; *Tr.*, reticulate tracheids. Camera lucida sketch (660 ×).

fibers. The tracheids vary from 65 to 85 microns in length and from 35 to 65 microns in width. The end walls are blunt or truncate, to slightly oblique. The markings on the walls are characteristically reticulate. Starch is found throughout the parenchyma and ray cells of the root. The starch grains are single, rounded to oval in shape and very small in size. The largest grains are rarely more than 7 microns in diameter, or along their longest axis, while the great majority are much smaller than this. A well-defined hilum is not apparent.

MICROSCOPY OF BEET ROOT.

The root of the beet, *Beta vulgaris* L., can be readily identified as an adulterant by the presence of large masses of parenchyma cells, showing no starch. Ramifying through these masses of cells are the reticulate tracheids. The parenchyma cells vary from 87 (or slightly less) to 130 microns in diameter. These are from two to three times the size of the horseradish cells. The reticulate tracheids occur in

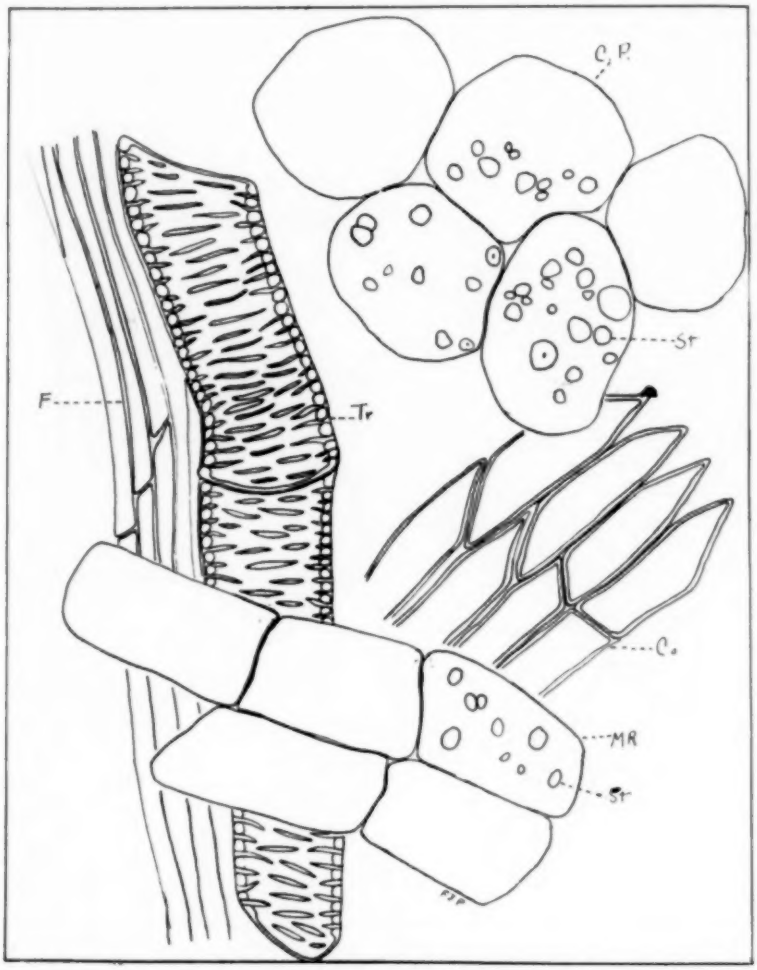

Fig. 4.—Parsnip Root (*Pastinaca sativa*). *Co.*, cork; *C. P.*, cortical parenchyma; *F.*, fibers; *M. R.*, medullary ray cells; *St.*, starch; *Tr.*, reticulate tracheids. Camera lucida sketch (660 ×).

masses, the individual tracheid ranging from 136 to 290 microns in length and from 17 to 26 microns in width, somewhat longer and narrower than those of horseradish. Thin-walled masses of elongated fibers accompany these vessels; these are upward of 200 microns in length and 9 microns in width.

MICROSCOPY OF WHITE TURNIP ROOT.

The white turnip, *Brassica rapa* L., if present in horseradish may be noted by its extremely large, thin-walled parenchyma cells devoid of starch. These cells

measure from 130 to 170 microns in diameter. The tracheids are shorter than either horseradish or beet, ranging from 80 to 120 microns in length and 30 to 50 microns wide. The markings are more rounded, of irregular size, giving the tracheid a very characteristic reticulate appearance. The vessels occur singly, or in small groups, in contrast with those of the beet and horseradish.

MICROSCOPY OF PARSNIP ROOT.

Parsnip root, *Pastinaca sativa* L., is characterized by the large numbers of single and compound starch grains present. The individual grains are rounded to slightly angular. The larger grains, 12 microns in diameter, show a centrally located cleft hilum. The compound grains occur in groups of two or three, with an occasional group of more than three. The angular grains are members of compound grains, separated during the grating process. The predominance of the larger grains, plus the presence of the compound grains, would serve to indicate the presence of parsnip in horseradish. The vessels of parsnip are of the usual reticulate tracheid type, ranging anywhere from 120 to 160 microns in length, and from 40 to 50 microns in width. The size would be midway between those of the horseradish and beet, and somewhat longer than those of the turnip. The vessels of parsnip are accompanied by extremely long, thin-walled fiber cells, averaging over 200 microns in length. The cortical parenchyma cells bear starch and measure about 64 microns in diameter. These cells are smaller than those of the beet and turnip, and larger than those of the true horseradish. Inter-radial parenchyma, medullary rays and tracheids occur combined in masses, in the grated state, both the ray cells and parenchyma cells bearing the above-mentioned starch.

Another added substance found in the commercial samples of horseradish was cornstarch.

SUMMARY.

	Parenchyma.	Stone Cells.	Tracheids.	Starch.
Horseradish	Isodiametic 48μ wide	Porous, striated, pale amber in color, 58 to 107μ long, 23 to 26μ wide	Reticulate 65 to 85μ long, 35 to 65μ wide	Simple 7μ broad
Beet	Isodiametric 87 to 130μ wide	Absent	Reticulate, 136 to 290μ long, 17 to 26μ wide	Absent
White Turnip	Isodiametric 130 to 170μ wide	Absent	Reticulate, 80 to 120μ long, 30 to 50μ wide	Absent
Parsnip	Isodiametric 64μ wide	Absent	Reticulate 120 to 160μ long, 40 to 50μ wide	Simple and 2 to 3 compound 12μ broad

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THE USE OF A HOSPITAL FORMULARY.*

BY ROBERT S. FUQUA.[1]

Hospital formularies have not been the subject of much discussion at previous AMERICAN PHARMACEUTICAL ASSOCIATION meetings, nor have many articles relating to them been published in the pharmaceutical press of this country. Questions regarding the use of such formularies have been discussed more frequently, and debated at greater length, at meetings of the Catholic Hospital Association than at those of any other nationally organized group.

It would seem that any discussion regarding the related questions of scope of such institutional publications and of the possibility of restricting prescribing in certain hospitals to the use of drug products listed in a formulary of this type would not be profitable or proper here. I believe however, that the purposes for which this Section of the A. PH. A. was organized can be promoted by bringing to this forum our ideas regarding the value of hospital formularies and any proven ideas which have been found to increase the value of these publications to physicians and patients in the particular hospitals which we happen to represent.

The statements made in this paper are not intended as an argument in favor of the use of a private drug-formulary in all hospitals. It is recognized by the writer, and by all others who have a fair knowledge of present conditions in the hospital field, that such a formulary would be of little value in many institutions, and of practically no value in those hospitals which do not employ a pharmacist at least on a part-time basis. I shall attempt rather to outline and comment on some of the more obvious advantages to be gained through the use of a private formulary in those hospitals having large resident staffs of physicians and surgeons, those which cater to large numbers of open-ward patients and those which maintain out-patient departments in which drugs are furnished to patients by the hospital pharmacist.

In listing possible advantages we must first consider the welfare of our hospital patients. Some of the criticism which has been leveled at the use of standard private-formula drug preparations in hospitals has been based on the assumption that they were usually cheap mixtures, intended in most cases to cover a variety of human ailments, and which were frequently prescribed because of cheapness rather than for any definite therapeutic efficacy. I know that most of the hospital physicians I have contacted over a period of years could justly resent the implication inherent in this assumption. I would say definitely that in the average hospital using a private formulary at this time the patient benefits equally with the physician and the hospital. In a busy hospital the standard made-up or quickly available standard extemporaneous preparations offer many advantages which need not be detailed at length. *First* in importance to the patient and the physician is the fact that prescribed treatment may be inaugurated promptly. The hospital physician seldom prescribes merely on snap diagnosis, except possibly to allay obvious pain, or other distressing conditions of a symptomatic nature. With his patient at ease he may proceed with orderly methods of diagnosis. To uphold his professional

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[1] Chief Pharmacist, Johns Hopkins Hospital, Baltimore, Md.

reputation he must make few mistakes in diagnosis; and his remedies and methods of treatment must produce results which compare favorably with those obtained by other physicians on a hospital staff. Under such circumstances a physician is likely to demand the drug or preparation which in his judgment is best suited to the condition of his patient, regardless of cost to the patient or to the hospital. In many cases however, the remedy chosen is a simple drug or a standard-formula hospital drug product, which will be either cheap or expensive as occasion demands. In such cases, the hospital usually benefits through lowered drug costs. Costs are paid by the patient; or by the public, which, in the final analysis pays the financial deficits of non-profit hospitals. More service to more patients at less cost is, or should be the goal of the administrators and the personnel of all public hospitals. The extent to which the pharmacist is rated as an important cog in the service organization of a well-managed hospital is usually proportional to the zeal exhibited by him in aiding in the attainment of this goal. A hospital formulary which standardizes and permits the quantity manufacture of such non-official mixtures and other pharmaceutical preparations as may be popular in individual hospitals will aid materially in reducing labor and costs for materials. Unnecessary costs which can be eliminated, and which permit a reduction in the amount of the average patient's bill are a potent factor in building up goodwill for the hospital.

Second, we must consider the needs of the physician who spends a large part of his time in hospital practice. I have commented previously on the compelling reasons these men have for demanding the best available medication, when drug administration is indicated. It is a generally accepted fact that physicians trained in any given medical school and allied hospital, or hospitals, will usually follow more or less well-defined methods of diagnosis and treatment. Prescriptions and simple or compounded drugs ordered will, at least in the early years of practice, conform rather closely to the ideas inculcated by certain medical school instructors and hospital-staff superiors. The result of this "follow the leader" tendency is shown in the numerous drug combinations of similar content ordered for the treatment of similar clinical conditions frequently encountered. The compounded preparations found in most hospital formularies are in the main simple adaptations of these frequently repeated prescriptions set up for quantity production, and are designed to reduce to a minimum the frequently unintentional quantity variations of two or more potent ingredients contained in these mixtures. In the larger hospitals a private formulary serves a real need in simplifying the prescribing of typical mixtures favored by groups of physicians treating patients in these institutions. Such formulas are usually simplified as much as possible to avoid undue labor in their preparation in the hospital pharmacy. These formulas are frequently used both as written, or as basic medication to which further additions of synergistic or modifying drugs may be made. The use of such standard-formula preparations saves the busy physician much time in the writing of prescriptions, and has the added advantage of preventing possible errors on the part of hospital internes who may on occasions be requested to write out prescriptions. Some staff physicians will refuse to accept the principle of majority rule in regard to the formulation of such mixtures or solutions, and will continue to write prescriptions for pet variations of standardized formulas. The more cheerfully we accede to the average physician's whims in respect to his pet combinations of drugs the less onerous will be the sum

total of his demands over a period of time. Some of the physicians who frequently seek and accept the writer's technical or therapeutic suggestions to-day are remembered as individuals who in earlier years more frequently demanded and received much unnecessary service.

In previous comments, intended to convey the idea that I believe a private formulary can be of real value in the majority of hospitals having representatives in this Section, I have omitted, except by inference, one of the important reasons for an earlier suggestion that ideas should be presented here which will aid us individually to be of help in improving some of the varied types of compilations known as formularies in hospitals. Most of us are in positions where the lack of knowledge of Materia Medica and prescription writing exhibited by hospital internes from a majority of the medical colleges is becoming increasingly apparent. I know of no more generally applicable method of unobtrusively advancing the cause of rational and economical drug-prescribing by our younger physicians than by disseminating needed information through the medium of a hospital formulary. If the hospital interne becomes sufficiently familiar with the use of standard drug preparations and simple mixtures listed in such a formulary, and acquires confidence in the value of these products in the treatment of disease, he will usually continue to specify these same drugs and preparations when he enters private practice. In most of the larger teaching hospitals a house formulary of some kind is now regarded as a necessity. As intimated before, these formularies vary widely as to scope and as to value to the institution whose needs they are intended to serve. Uniformity in these respects is not to be hoped for. In respect to contents I do not believe uniformity would be desirable in different independently operated hospitals. For the hospital interne the formulary used in an institution should be a booklet of carefully considered information, which will supplement in some measure his meager knowledge of the proper methods to use in combining or dispensing in effective and palatable form the simple drugs which he has been taught are of therapeutic value.

We are all familiar with the incomplete and ambiguous type of prescription which so often comes to the institutional pharmacy. We become accustomed to this in our daily routine. In most cases we can prevent the lengthy periods of waiting for medication which the patient would frequently face if such prescriptions were written outside of the hospital. Few of us, however, can overcome a certain feeling of chagrin when such prescriptions are sent out of the hospital to our friends in retail pharmacies. Our sense of pride in our institutions is ruffled, and we wonder vaguely how this form of bad advertising might be at least lessened in so far as our particular hospital is concerned.

As pharmacists we are not responsible for the inadequate training received by medical students in the matter of prescription writing. We can only hope for a change in the curriculum of the medical schools. Personal help or advice to a few individual internes is the full extent of personal effort we may exert to correct this condition in most hospitals. Aside from this, our formularies appear to be the most readily available tool with which to work. In many of our hospitals to the necessary costs of treatment for private patients, increasingly onerous charges for expensive proprietary drug products must be added. The majority of our visiting

physicians order much of this material because of a lack of confidence in their ability to write prescriptions for wanted drugs in equally acceptable forms. Hospital formularies would help some hospitals to cut down on unusually high drug charges to patients if the use of such publications could be inaugurated. Improvement in inadequate formularies now in use in some other institutions, with aid to the hospital interne as a guiding principle, should provide some of us with additional opportunities for service.

A FURTHER STUDY OF TINCTURE OF CANTHARIDES.*

BY L. M. OHMART[1] AND E. T. MORGAN.

At the 1936 meeting of this ASSOCIATION, the senior author submitted a paper entitled "A Preliminary Study of Tincture of Cantharides" (1) to the Section on Practical Pharmacy and Dispensing. The paper reviewed the changes which have been made in the official formula for this preparation in the attempt to devise a method of preparation and a menstruum which would yield a satisfactory tincture.

The investigations of Squibb (2), Scoville (3, 4, 5, 6), Nitardy (7, 8, 9) and Eberhardt (10) were briefly reviewed. As a result of these investigations, notably those of Scoville, the menstruum for the present official tincture contains 10% by volume of glacial acetic acid. Numerous criticisms of the present official preparation have been voiced, chiefly on account of its strong acetous odor. Because of these criticisms, the senior author undertook to devise a method which would yield a preparation free from these objections. The earlier paper reported the results obtained from thirteen experimental tinctures. It was found, as earlier investigators had reported, that alcohol was unsuitable as a menstruum; that mixtures of alcohol and glacial acetic acid gave better results; that a menstruum containing 10% of the acid was better than those of lower concentration. It was further found that mixtures of hydrochloric acid and alcohol were superior to mixtures of glacial acetic acid and alcohol in the extraction of cantharidin. The official process of maceration was found to be superior to the official process of percolation as a method of extraction for cantharides. To confirm the results previously obtained, and to establish the minimal concentration of hydrochloric acid in alcohol as a menstruum for tincture of cantharides, the present study was undertaken.

EXPERIMENTAL.

Two lots of cantharides were procured and were assayed by the U. S. P. method. Drug A, a fine powder, yielded 0.803% of cantharidin. Drug B, a fine powder, yielded 1.029% of cantharidin. Fourteen tinctures were prepared from Drug A and were assayed according to Scoville's (4) modification of the method of Self and Greenish (11). The methods of preparation, menstruum used and assay results are shown in Table I.

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* Presented before the Section on Practical Pharmacy and Dispensing, A. PH. A., Minneapolis meeting, 1938.

[1] Massachusetts College of Pharmacy, Boston, Mass.

TABLE I.

Method.	Menstruum.	Cantharidin Content. Maximum 0.0803 Gm.	Percentage of Extraction.
1 Percolation	Alcohol + 0.25% HCl*	0.0623 Gm.	77.5%
2 Percolation	Alcohol + 0.50% HCl	0.0613 Gm.	76.3%
3 Percolation	Alcohol + 0.75% HCl	0.0695 Gm.	87.0%
4 Percolation	Alcohol + 1.00% HCl	0.0711 Gm.	88.5%
5 Percolation	Alcohol + 1.50% HCl	0.0648 Gm.	80.7%
6 Percolation	Alcohol + 2.00% HCl	0.0628 Gm.	78.2%
7 Percolation	Alcohol + 2.50% HCl	0.0617 Gm.	76.8%
8 Maceration	Alcohol + 0.25% HCl	0.0641 Gm.	79.8%
9 Maceration	Alcohol + 0.50% HCl	0.0587 Gm.	73.1%
10 Maceration	Alcohol + 0.75% HCl	0.0728 Gm.	89.9%
11 Maceration	Alcohol + 1.00% HCl	0.0713 Gm.	88.6%
12 Maceration	Alcohol + 1.50% HCl	0.0541 Gm.	67.3%
13 Maceration	Alcohol + 2.00% HCl	0.0486 Gm.	60.4%
14 Maceration	Alcohol + 2.50% HCl	0.0593 Gm.	73.8%

* Percentages are of the absolute acid.

While a menstruum of hydrochloric acid and alcohol is equal to or superior to one of glacial acetic acid and alcohol in its power to extract cantharides, there are two objections to its use. It extracts a considerable quantity of material which is deposited on standing and bottles in which tinctures made with this menstruum are stored soon acquire a coating which is unsightly.

Further investigation was undertaken in the hope of discovering a menstruum which would provide a tincture free from these objections while efficiently extracting the cantharidin. A menstruum of lactic acid and alcohol was chosen for these experiments. Ten tinctures were prepared from Drug B and were assayed by the method before stated. The methods of preparation, menstruum used and assay results are shown in Table II.

TABLE II.

Method.	Menstruum.	Cantharidin Content. Maximum, 0.1029 Gm.	Percentage of Extraction.
1 Percolation	Alcohol + 1% $CH_3 \cdot CHOH \cdot COOH$*	0.0939 Gm.	91.3%
2 Percolation	Alcohol + 2% $CH_3 \cdot CHOH \cdot COOH$	0.0867 Gm.	84.3%
3 Percolation	Alcohol + 3% $CH_3 \cdot CHOH \cdot COOH$	0.0987 Gm.	95.9%
4 Percolation	Alcohol + 4% $CH_3 \cdot CHOH \cdot COOH$	0.0925 Gm.	90.0%
5 Percolation	Alcohol + 5% $CH_3 \cdot CHOH \cdot COOH$	0.0936 Gm.	91.0%
6 Maceration	Alcohol + 1% $CH_3 \cdot CHOH \cdot COOH$	0.0794 Gm.	77.2%
7 Maceration	Alcohol + 2% $CH_3 \cdot CHOH \cdot COOH$	0.0920 Gm.	89.4%
8 Maceration	Alcohol + 3% $CH_3 \cdot CHOH \cdot COOH$	0.0899 Gm.	87.4%
9 Maceration	Alcohol + 4% $CH_3 \cdot CHOH \cdot COOH$	0.0885 Cm.	86.1%
10 Maceration	Alcohol + 5% $CH_3 \cdot CHOH \cdot COOH$	0.0850 Gm.	82.6%

* Percentages are of the absolute acid.

The tinctures obtained in the foregoing experiments were brilliant liquids of a brownish green color. No deposition had occurred after two months and their brilliancy was unimpaired. No foreign odor was perceptible. In all of the experiments reported in this paper, in which the process of percolation was employed, the drug was mixed with five times its weight of purified sand and the percolation was allowed to proceed at a very slow rate. Subject to these modifications, the process of percolation was found to be superior, in most cases, to the process of maceration in extracting cantharides.

SUMMARY AND CONCLUSIONS.

1. A paper on this subject, presented by the senior author in 1936, is briefly reviewed.

2. Experiments were conducted in an attempt to confirm the results previously reported and to determine the optimum concentration of hydrochloric acid in a menstruum for tincture of cantharidin.

3. The optimum concentration of hydrochloric acid was found to be approximately 1% of the absolute acid.

4. Certain objectionable features of tinctures in which hydrochloric acid had been used led to further investigation.

5. A menstruum of lactic acid and alcohol was found to be fully as efficient as one of hydrochloric acid and alcohol and the tinctures so prepared were not objectionable in odor or appearance.

6. The optimum concentration of lactic acid was found to be approximately 3% of the absolute acid.

7. A modified process of percolation was found to be superior to the process of maceration in extracting cantharides.

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THE VALUE OF VARIOUS PROMOTIONAL METHODS FOR PRESCRIPTION PHARMACIES.*

BY M. A. CHEHAK.[1]

In a discussion of promotional methods for prescription pharmacies, it is first necessary to reminisce and visualize the tremendous change that has taken place in Pharmacy as a whole within the last twenty years. Considering that Pharmacy is one of the oldest professions, it is only within the last few years that the pharmacist has made any concerted effort to prove his service in the interest of public health to the public. The layman is aware of the division of professional pharmacy and commercial pharmacy, but it seems that the pharmacist has been a little lax in his professional promotional efforts.

I am sure if we, as professional pharmacists, will take the physician's viewpoint as to what he considers ethical promotional methods, the problem will not seem so difficult. In directing our promotional work the physician's viewpoint has always been uppermost in our minds.

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* Presented before the Section on Practical Pharmacy and Dispensing, A. PH. A., Minneapolis meeting, 1938.

[1] 730 Merchants Nat'l. Bk. Bldg., Cedar Rapids, Iowa.

It is granted that the professional pharmacy first must look the part. Both the exterior as well as the interior of the store must have a professional atmosphere and made to appear like a scientific chemist shop, such as is found in England.

One of our stores is located above the ground floor close to the offices of physicians and we have called this shop a LABORATORY rather than a pharmacy. Our street store uses a large neon sign with the caption "PRESCRIPTION CHEMISTS," which identifies our store as a professional pharmacy. After four years of required college training, the druggist is more in name and training than a pharmacist. He is a pharmaceutical chemist and so we have carried this thought to the patient.

We believe there are at least three requisites for the interior for professional atmosphere, namely: *first*, that there be an inviting reception room with comfortable seating facilities, or at least a comfortable seating arrangement for the patient while waiting for the prescription; *second*, that an attractive, well-planned, open-view prescription laboratory work-table be in plain view and possess considerable professional dignity; *third*, a complete pharmaceutical library and conference room, if space is available.

The pharmacist who maintains a professional pharmacy must be a student at all times, because of the large number of new medicinals and chemicals that are being offered every day. It is difficult to appreciate how pharmacists can properly conduct a professional institution without at least a technical library at his command which should include medical journals as well as pharmaceutical literature. It should be unnecessary to mention that complete equipment including analytical balance, automatic water still, clean glassware, capsule-filling machine, clean mortars, pestles and show globes, all tend to promote professional atmosphere.

Now that we have shown the physician that we have a pharmaceutical laboratory such as he would like us to maintain, what professional service are we going to render him and promote this service? Twenty years ago we thought that a complete prescription and chemical laboratory service was about all that was necessary. To-day we aim to be responsible for every type of service which the modern physician needs. This, of course, covers a great deal of territory but here are a few of the things we supply daily to our physicians:

A complete prescription service is maintained by five college graduates including pharmacists, clinical pathologist and pharmaceutical chemists, and a complete laboratory service which includes all types of blood examination, urinalysis, serology work, bacteriological examinations such as typing of blood and pneumonia groups and the manufacture of autogenous vaccines. Complete gas anesthesia service is maintained such as supplying ethylene, nitrous oxide, cyclopropane, resuscitation gas and oxygen therapy for heart and pneumonia cases. We maintain a complete service in surgical appliances such as elastic stockings, braces, trusses, post-operative garments and supports—a service which the physicians do appreciate. A complete biological service is maintained supplying physicians anti-toxins, serums, liver extracts, typing serums and diagnostic biological reagents such as blood typing sera, tuberculins and other antigens. Surgical dressings, gauze, zinc oxide tape, cotton, plaster splints and all types of metal splints are available to the physician and constitute a large part of the physician's daily needs.

Delivery service is available day and night and sometimes is most important of all. The patient that is hospitalized or confined at home appreciates this personal service. And this we stress to the physician as part of our daily duty to him and his patient.

We maintain a complete equipment service for the physician that is starting practice, and although we don't have a large stock, we are able to supply the physician with instruments of all descriptions—sterilizers, laboratory apparatus such as microscopes, colorimeters and reagents—in other words we have told our physicians that we can supply their needs in any type of service that they may be confronted with no matter what may be required. This complete service to the physician is the most valuable promotional effort of the professional pharmacist.

Now that we have a truly professional pharmacy and a complete service to the physician, what methods are to be used in our promotional efforts? Obviously, the form letter is one of the primary features. Postal cards describing new products keep the physician mindful of our prescription department. Promotional letters, both to the laity as well as to the physician must be a part of your continuous effort as this is one of the most efficient ways of bringing new products to his mind and is a reminder of your desire to serve.

Direct promotional sales or detailing must be considered as one of the most successful methods. One of our eleven employees is almost always in contact with some physician concerning one of the many services we offer. A personal call is often made regarding a clinical diagnosis and a discussion often follows as to the patient's medical needs. Some special instrument is often required and we visit the physician showing him our list of instruments or, if certain specifications or manufacture are desired, we supply his needs. In these personal contacts we endeavor to stress products of our own manufacture and also the research work that we constantly carry on. We are continually working on some pharmaceutical problem and these are brought to the attention of the physician—such as a new vehicle for a prescription, a new product for Vincent's angina, or a new topical anesthetic that we have brought out to the dentist as constant reminders that we are pharmaceutical-chemists and capable of compounding his prescriptions in a professional way.

Now let us consider the patient or, the LAITY, as you choose. For ten years we have used small newspaper "Health Talks," usually placed on the editorial page, directing the patient to visit a physician when medical attention is needed. In this way we have created good-will from the physician. In turn we ask the patient that we, as ethical pharmacists, be allowed to fill his prescription needs.

About two years ago we sponsored a radio broadcasting program over WMT called the "LIFE SAVERS." Starting with a thirteen-week contract we continue the programs which consist of a dramatized ten-minute sketch on some medical or pharmaceutical incident. Originally the programs were individual sketches illustrating some particularly interesting incident in modern or historical medicine reflecting credit on the profession. Later a longer series was run on the history of Medicine from the early up to the present time. Another series on the life of Clara Barton, the Red Cross Nurse, was run successfully as far as creating interest was concerned, and also a story of Louis Pasteur inspired by the movie production.

In the opening announcement of these broadcasts, attention is called to the work done by modern medical life savers and the public is urged to always see the

doctor first. In the series our two ethical prescription pharmacies are tied in as the safe place to fill that important prescription. The program, given weekly, goes on usually at 6:P.M., Monday. Cards in the two pharmacies call the public's attention to the "LIFE SAVERS" broadcasts and displays of pharmaceuticals have been placed advantageously in the broadcasting lobby and likewise in the two stores.

We realize that only a few pharmacies will be situated in such a way as to use the radio with a program so pretentious. It has proven to be, without doubt, the finest promotional endeavor we have tried, although no product of any type is mentioned nor does the price enter into the program.

While this radio program advises the patient to see a physician regularly, we also endeavor to tell the public that a prescription may be expected when a physician is consulted. We try to make the laity conscious of the fact that each person should be treated as an individual and to expect the physician to prescribe for them instead of dispensing. It is, of course, impossible to estimate the value of this type of promotional radio program in dollars and cents as good-will is created with the physician as well as the public. However, I do know that it has doubled the number of our prescriptions filled and has made our physicians more prescription-conscious.

THE ASSOCIATION FOR THE ADVANCEMENT OF PROFESSIONAL PHARMACY.

The regular monthly meeting was held Tuesday, March 28th, Hotel Dauphin, with about 150 present. At this meeting Dr. J. Leon Lascoff, president of the AMERICAN PHARMACEUTICAL ASSOCIATION, was elected a fellow in recognition of his forty years of work in professional pharmacy.

Prof. Abraham Taub, Columbia University College of Pharmacy, gave an excellent talk on "Ophthalmic Solutions." Dr. S. A. Agatson, New York University Medical School, and Dr. Cosmo Ligorio, Brooklyn College of Pharmacy, led the discussion following. Other speakers included Dr. H. V. Arny, dean emeritus, Columbia College of Pharmacy, and Milton Malakoff, editor, *New York State Pharmacist*.

The fourth meeting was held April 18th, with 150 in attendance. Minutes of the previous meeting were read, followed by the report of the treasurer and of the various committees.

Miss Mary Grace conducted a symposium on "Hospital Pharmacy." The speakers were: Miss Mary Grace, "Practice of Pharmacy in Hospitals;" Miss Mary Crofa, "Exhibition of U. S. P. and N. F. Preparations in the Hospital;" Leo Reich, "Uplifting of Professional Pharmacy by the Hospital Pharmacist;" Morris Dauer, "Teaching Hospital Pharmacy in the College of Pharmacy."

Sister Jenette of Mary Emaculate Hospital prepared and presented an excellent display on the iron and ammonium citrate sales used in U. S. P. and N. F. propaganda work among the physicians.

The fifth meeting was held on May 16th, with ninety-four present. Mr. O. U. Sisson of Chicago was guest speaker. He discussed pharmacy organizations and the need of more organization in professional Pharmacy. Mr. Sisson has volunteered to help in the organization of various Chapters throughout the mid-west.

Other members and guests who spoke were: Dr. J. Leon Lascoff, president of the A. PH. A., Dean C. W. Ballard of Columbia College of Pharmacy, Mr. K. W. Unsworth, president of the Westchester County Pharmaceutical Association and Mrs. May O'Connor Davis, secretary of the same Association. Prof. F. D. Lascoff of Columbia University College of Pharmacy continued the series of instructive lectures which have been a feature of the Association meetings with a talk on "The Business Problems of the Professional Pharmacy."

Several manufacturers and specialists in professional pharmacy window displays presented a series of actual full-sized window displays suitable for a professional pharmacy.

IRVING KANTOR, *Secretary*.

PROCEEDINGS OF THE LOCAL AND STUDENT BRANCHES

BALTIMORE.—The last meeting of the Spring season was held on Thursday evening, May 25th, at the School of Pharmacy Building, University of Maryland, at 8:30 P.M.

The guest speaker of the evening was Dr. J. A. Morrell, who is now conducting studies on endocrine products at the Squibb Institute for Medical Research, New Brunswick, N. J., and who spoke on, "Some Recent Advances in Endocrinology." The address proved of interest and value to all pharmacists who heard it, and especially as endocrine products are being prescribed in constantly increasing numbers and volume by practicing physicians.

Refreshments were served at the conclusion of the regular meeting.

ROBERT S. FUQUA, *Secretary.*

CONNECTICUT COLLEGE OF PHARMACY STUDENT BRANCH.—On January 13, 1939, the first meeting of the proposed Student Branch was called to order by temporary chairman, Abraham Wolfthal. The following officers were elected: *President*, Abraham Wolfthal; *Vice-President*, Milton Zimmerman; *Treasurer*, Jack Kraut; and *Secretary*, Charles Blumenthal.

A general discussion of the constitution was held and, with a few revisions, was adopted. The president selected a Program Committee charged with the preparation of a program for an installation meeting. The treasurer was instructed to arrange for the collection of fees, and a date was set for remittance of all necessary matter for approval of the branch to Dr. E. F. Kelly, secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION.

On May 10th the installation meeting was held at the College. The first part was devoted to business.

Beginning the open meeting with an address of welcome, President Abraham Wolfthal introduced Dean Henry S. Johnson who extended the welcome of the college to all present. Dr. Hugh P. Beirne and Mr. Clark H. W. Newton, trustees of the college, were asked to address the group and responded handsomely.

At this point a message from Dr. J. Leon Lascoff was read to the assembly, by the president. Then, under the direction of Prof. Leslie B. Barrett and Instructor Nicholas W. Fenney, the officers and members of the branch were officially installed and presented their charter.

The president then introduced the guest speaker for the evening, Dr. Robert C. Page, medical advisor, Burroughs Wellcome & Co. Dr. Page discussed various new chemotherapeutic agents, among them, Vitamin B_6, Magnesium Trisilicate as an antacid agent, the alkaloids of Ergot, the male and female sex hormones and the therapeutic problems of Sulfapyridine as to toxicity and tolerance. The talk was concluded with a film and commentary on the assay of vitamins. A discussion period followed, and a rising vote of thanks to Dr. Page was given.

CHARLES BLUMENTHAL, *Secretary.*

FERRIS INSTITUTE STUDENT BRANCH.—The meeting was held March 8th with President Ida Mary Fox presiding. Minutes of the last meeting were read and approved.

After a short business session the meeting was turned over to Mr. Engmark, who introduced the speaker of the evening, Mr. O. F. Swoap, director of the Assay Department of the Upjohn Co. Mr. Swoap gave a very interesting talk on "The Assay of Digitalis by the One-Hour Frog Method." In the discussion it was pointed out that the frogs are of uniform weight and stored in tanks of running water prior to injection. They are divided into two groups, one is injected with different dilutions of a standard digitalis preparation in the ventral lymph sac while the second is injected with dilutions of the unknown digitalis preparation. Fifty-eight minutes after making the respective injections each frog is pithed. Each heart is exposed and examined at exactly one hour after the injection, determining the number in each dosage group in which the ventricle is in systolic standstill, or passes into systolic standstill on gentle mechanical stimulation. In the typical positive reaction the ventricle is in systolic standstill while the auricles are widely dilated. By comparing the activity of the preparation being assayed with the reference preparation necessary adjustments are made so that the finished product will conform to the required biological standard.

A motion picture of the actual assay by the one-hour frog method was shown during the lecture.

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The April meeting was held at Ferris Institute on the 5th.

The speaker of the evening was Dr. Rogers, a local dentist. Toothpastes were discussed and it was pointed out as one of the best rackets in the country. Many toothpastes and mouth washes are good but do not live up to the claims of the manufacturer so are condemned by the American Dental Association. Dr. Rogers stated that the pharmacist can do a great service to the customer by telling of these frauds in dentifrices and by recommending the good products. Denture adhesives are frowned upon by the dental profession because the tragacanth in these adhesives causes excessive flow of saliva which in turn causes gums to become soft and spongy.

Dr. Rogers described the lastest methods used in combating tooth decay. A mixture of oil of cloves, peppermint oil and wintergreen oil is as good as any medicine for toothache. The trouble with most patent medicines is that they are highly escharotic. Toothache gums are not prescribed for the teeth as they only cause an increased aching.

Trench mouth was discussed and it was pointed out sodium perborate will not stop trench mouth because the bacteria become immune to it and afterward grow in it. The cause of recurrence is due to the fact that it is not properly cleaned up as bacteria may work down under an overlapping filling and live there, or lodge between the teeth. Sodium perborate if used in excess for mouth washes, may cause chemical burns, edema or hairy tongue.

A very interesting discussion followed.

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The May meeting was held May 3rd at Ferris Institute. Having disposed of all business, the meeting was turned over to Mr. Engmark, who had the pleasure of introducing the speaker of the evening, Mr. E. H. Krantz, sales manager of the Detroit district of Eli Lilly and Co.

Mr. Krantz chose for his topic "The History of Antiseptics." He related the story of antiseptics starting with the Egyptians hundreds of years before the birth of Christ. He told of their increased importance and improvement during the middle ages up to the present day. A brief résumé of the lives and work of such famous men as Joseph Lister and Louis Pasteur was outlined. The speaker lent a considerable portion of his time to the discussion of modern antiseptics and the tests and standards for these antiseptics. The shortcomings and the good points were emphasized.

Following the talk Mr. Krantz led a lively discussion and answered questions on antiseptics.

LESLIE KIEFT, *Secretary.*

GREATER ST. LOUIS.—The last meeting of the year was held on May 8th at the St. Louis College of Pharmacy. This was a business meeting and was intended to bring out suggestions for increasing attendance and to formulate plans for next year. Two definite proposals were decided upon: (1) The meetings will be held in a hotel at 6 o'clock with a dinner preceding the scientific discussion; (2) The speakers will include members of the local branch and will represent both scientific and commercial subjects.

A letter from Dr. E. F. Kelly, concerning the AMERICAN PHARMACEUTICAL ASSOCIATION exhibit at the American Medical Association Convention in St. Louis, was read. Plans were made to provide for attendants at the booth and for the preparation of the National Formulary display.

FRANK L. MERCER, *Secretary.*

LOYOLA UNIVERSITY STUDENT BRANCH.—The annual banquet and dance was held at Arnaud's Restaurant on Thursday, May 4th, at 8:30 P.M. Addresses were made by Rev. Edward T. Cassidy and Very Rev. Harold A. Gaudin. Over two hundred pharmacists of the city of New Orleans were present, and the thirty-seven members of the Branch showed up 100%. Toastmaster for the occasion was a freshman, Mr. Herbert J. Mang, who did so splendidly that he kept his audience wondering.

Two weeks before the banquet the annual election of officers was held, resulting as follows: *President,* John F. Thompson; *Vice-President,* Nicholas Montalbano; *Recording Secretary,* Miss

June Ware; *Corresponding Secretary*, Joseph Hecker; *Treasurer*, Herbert Mang. The salient feature at the banquet was the induction of these officers to serve during the year 1939–1940. Preceding the installation of new officers the old officers who had served the Branch so faithfully were presented, and the retiring president, Mr. Babin, took the opportunity of thanking the officers for their fine support and splendid coöperation, and also expressed the gratitude of the Branch for the support and coöperation given by the wholesale and retail pharmacists, which led to the success of this event. The new officers were then called to the stand and having been officially installed pledged their loyalty for the year to come. Mr. Lauve, installation officer, pointed out the progress of Pharmacy which the AMERICAN PHARMACEUTICAL ASSOCIATION is promoting.

At the conclusion of the banquet Honor Awards were made to Miss Elsie Strain and Mr. Joseph Ernst. Following the banquet the evening was concluded with a dance under the supervision of Miss Helen Pitre and Mr. Paul Poche.

NICHOLAS MONTALBANO, *Corresponding Secretary.*

MICHIGAN.—The April meeting was held at the Wayne County Medical Society Headquarters, April 28th, preceded by a dinner. Minutes of the previous meeting were dispensed with, since they are published in the JOURNAL.

The main portion of the program was devoted to original papers presented by students of three colleges of pharmacy in Michigan. The discussion which followed proved their excellence. They were as follows: Donald Creagan, University of Michigan, "An Introduction to Sulfapyridine;" Harry Hayes, Detroit Institute of Technology, "An Investigation of Devil's Club Bark;" Mr. Schuler, Wayne University, "The Oxidation Rancidity of Oils."

Mr. R. L. McCabe opened discussion of Mr. Hayes' paper, requesting more information regarding the Indian. It was stated that the Indian could not be regarded as a true test of the drug, since there are no controls. Mr. L. A. Seltzer stated that an increase in the dose of Devil's Club Bark reverses the effects of the drug; also that he uses egg whites instead of lead to precipitate the tannins. Prof. C. C. Glover advised that a drug similar to Devil's Club Bark has been found but has not been reported in literature. Dean Lakey asked Dr. Emmert whether he could tell what happens to the burned-up sugar and Dr. Emmert related the incident of the lady in the Eloise Infirmary whose sugar went down when she was allowed to chew tobacco. It was discovered that codeine phosphate was incorporated in the tobacco. Later she developed carcinoma of the liver. An autopsy revealed an increase of liver cells.

Mr. Seltzer commented on the dangers of sulfapyridine. Mr. Creagan asserted that the drug is less toxic than sulfanilamide. Dr. Ashworth pointed out that in cases of pneumonia only typed cases can be given the drug or serum. The serum is effective in all but Group III. Mr. Webster wondered as to the high cost of sulfapyridine and Mr. McCabe advised that other serums cost much more and that the retail price for fifty capsules of sulfapyridine, $6.75, is not much.

Dean Lakey asked for a discussion of the proposed increase in retail pharmacy license fees. Mr. Seltzer expressed his opinion that the increase in fees was for the better policing of the pharmacists and that, since it was for the protection of the public, why shouldn't the public pay for such protection. Also, it was pointed out that the fees paid by pharmacists have heretofore been absorbed into the general state budget. Mr. Seltzer moved that the Michigan Branch go on record as opposed to the proposed increase in pharmacy fees, and the motion carried.

The worth of the program was greatly enhanced by the comments of Dr. Ashworth, and Mr. Webster expressed the desire of the membership that more physicians take a part in the future meetings of the Branch.

A rising vote of thanks was accorded the student speakers.

MORRIS ROGOFF, *Acting Secretary.*

NEW YORK.—The last regular meeting for the spring season was called to order at 8:45 P.M., May 8th, at Columbia University College of Pharmacy. President Canis presided, and about seventy-five members and guests were present. Minutes of the April meeting were approved as read.

Report of the Secretary of the Remington Medal Committee was: There are 18 members of the Remington Medal Committee entitled to vote. Candidate A received nine votes; Candidate B, seven votes; Members not voting, two. Since the rules require the successful candidate to receive a majority of possible votes, in this case ten, the tellers declare that neither candidate has received a majority and neither has been elected.

A communication from Secretary Kelly advises that consideration will be given a proposal by the Branch to have future N. F. Supplements printed in the JOURNAL, and that in any instance due notice of changes will be given in the JOURNAL.

There being no further business, the meeting turned to the Scientific Section. Mr. Gustave Bardfeld acted as chairman and introduced Dr. Cary Eggleston, Associate Professor of Clinical Medicine, Cornell University, Medical College, who discussed "Digitalis and Its Glucosides;" and Dr. Arthur C. De Graff, Professor of Therapeutics, New York University, College of Medicine, who discussed "Diuretics Used in Cardiac Conditions."

Displays of drugs used in cardiac conditions were offered by E. R. Squibb & Sons and by the Lederle Laboratories. A display of appropriate U. S. P. and N. F. preparations was shown by Mr. Frederick D. Lascoff.

At the conclusion of a considerable discussion, a rising vote of thanks was accorded the speakers.

HORACE T. F. GIVENS, *Secretary.*

NORTHERN OHIO.—A regular monthly dinner meeting was held at the Faculty Club of Western Reserve University at 6:30 P.M., April 14th.

After reports by chairmen of standing committees and remarks by members of the Branch, President Stonebraker introduced Dr. Leonard G. Steuer, Senior Instructor in Medicine, Western Reserve University, as the guest speaker. He discussed the action and uses, the side reactions and dangers involved in the use of the first four drugs to be placed on the dangerous drug list by the Federal government; namely, sulfanilamide, amidopyrine, cinchophen and neocinchophen.

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The May dinner meeting was held at the same place on May 12th.

After some discussion of routine business affairs, Dean Spease of the School of Pharmacy led a discussion of the more significant features of the Federal Food, Drug and Cosmetic Act which will become fully active on the 25th of June. Some of the distinct advantages which the new act has over the old were pointed out in detail, especially the extension of formula disclosure and the warning label requirements.

Dr. Einar J. Olsen was introduced as the guest speaker of the evening. His subject was "A Chalk Talk on Dentistry." He aptly sketched some of the details of normal tooth structure and malformation. With the sketches as a background he then elaborated upon some of the useful and useless forms of mouth medication from the viewpoints of both Denistry and Pharmacy.

N. T. CHAMBERLIN, *Secretary.*

PHILADELPHIA.—The May meeting was called to order at 8:P.M. on May 9th at the Philadelphia College of Pharmacy and Science. Minutes of the April meeting were read and approved.

Chairman Osol outlined the program for the evening, and introduced the first speaker, Dr. Chas. E. Vanderkleed of the McNeil Laboratories. He reviewed the development of Food and Drug legislation, comparing the adoption of the 1906 Act with the present unsettled transition. Dr. Vanderkleed considers the new act satisfactory as long as considerate administration is continued, but advised that due to the many phases subject to regulatory features, it could become very burdensome if those responsible for its enforcement became supercritical. He mentioned that it differed from the 1906 act in that it covered cosmetics and devices, included a "new drug" provision, and provided for libel action against items bearing statements that were false *or* misleading as compared with the present (1906) act that requires that the statement be false *and* fraudulent.

Dr. Vanderkleed then discussed individual sections of the act, covering the more definite points only briefly, but going into some detail regarding the less understood sections. He spoke about "Titles" as covered by Section 502A of the "regulations," commenting on the differ-

ence between the present opinion of the Department with that of Dr. Harvey W. Wiley. Dr. Wiley considered nomenclature similar to that used by the official compendiums as suitable. He believes the Department's present dislike for the word "compound" as a part of the title of a preparation composed of many ingredients leads to the coining of fanciful, meaningless names and subsequent confusion.

Dr. Vanderkleed mentioned that Section 502B contains no satisfactory exemption for small packages of drugs. He warned that one must keep the difference between "label" and "labeling" clear in mind, and that statements required on the label must be on the front panel, even at the sacrifice of trade marks or other distinctive features of long standing.

Dr. Vanderkleed stated that Section 502f would offer the greatest problems, for the labeling must bear (1) adequate directions for use; and (2) such adequate warnings against use in those pathological conditions or by children where its use may be dangerous to health, or against unsafe dosage or methods or duration of administration or application, in such manner or form, as are necessary for the protection of the users. The difficulty is in arriving at an opinion as to what constitutes an adequate warning for such drugs as cinchophen, acetanilid, laxatives, etc.

Dr. Munch, of Munch Laboratories, was then introduced and he discussed at length the important part the pharmacologist plays in the present set-up, in testing toxicity and habit formation of drugs, and development of new drugs. He then discussed what constitutes a "new drug" and the steps required to comply with Section 505 of the new act.

A lengthy discussion followed, chiefly as to the effect of the new law on the retailer if he were to introduce a prescription in interestate commerce or dispense an item over the counter which was labeled "Caution: To be used only by or on the prescription of a physician." No definite conclusions were reached on these points.

Dr. J. W. E. Harrisson of LaWall & Harrisson, who was to be the third speaker, was unable to attend in person, but sent a very interesting and humorous telegram which was read to the group by Dr. Osol. He also sent mimeographed copies of interpretations of the act.

A rising vote of appreciation was accorded the speakers.

R. H. BLYTHE, *Secretary.*

PITTSBURGH COLLEGE OF PHARMACY STUDENT BRANCH.—A meeting was held in the Pittsburgh College of Pharmacy, April 6th, at which Mr. Nosidlak, retiring president, presided. The newly elected officers, George Kelly, secretary, Victor Bianculli, vice-president and Harry Bonchosky, president, were installed and a short program presented by members of the student body followed.

The first speaker, Mr. Silvestri Silvestri, gave a very interesting talk on the History of the Pittsburgh College of Pharmacy from the time of its origin up to the present day. The second speaker, Mr. Fred Reif, gave a brief but very concise report of the newly passed Pure Food, Drug and Cosmetic Act of 1939. Mr. Reif dealt chiefly with those phases of the law which have a direct influence on the pharmacist and his pharmacy. The last speaker, Mr. Victor Bianculli, spoke on "The Open Prescription Counter." Mr. Bianculli discussed the advantages and disadvantages of this type of counter in modern pharmacy. Dean O'Connell gave brief comments on each of the talks.

GEORGE M. KELLY, *Secretary.*

A public hearing, for the purpose of receiving evidence upon the basis of which regulations may be promulgated amending those appearing in the *Federal Register* for May 9th by changing certain specifications of some of the listed colors and adding other coal-tar colors to the list, will be held on July 5, 1939, at 10:00 A. M., Room 1039, Department of Agriculture.

All interested persons are invited to attend, and if this is impossible affidavits may be mailed so as to be received not later than July 5th, to Mr. Frank S. Hassell, Room 2313(A), South Building, Department of Agriculture.

The new coal-tar colors proposed for addition and the changes in specifications, are published in the June 3, 1939 issue of the *Federal Register*, which will be mailed on receipt of 10¢ from the Superintendent of Documents, Government Printing Office, Washington, D. C.

PERSONAL AND NEWS ITEMS.

Wm. B. Scaife & Sons Co., of Pittsburgh, has established an industrial fellowship in Mellon Institute for the purpose of conducting scientific research on problems pertaining to processes of fabricating and to the use of metal tanks, pressure cylinders, and water-softening equipment, its principal products. This investigational work will be in accordance with the company's desire to keep closely informed regarding all technical progress in its own and related fields, with special attention to present and probably future trade requirements, and to effect through research and development all possible improvements in its production practice as well as its products. For many years the company has carried on technical studies in its own organization, but the fellowship at Mellon Institute will enable the Scaife scientific staff to benefit by the investigational and cooperative facilities of the Institute. **Dr. H. L. Anthony, III,** is the incumbent of this fellowship.

The Wyoming Pharmaceutical Association met on May 22nd and 23rd at Torrington. A fine program was carried out. Among the speakers were: Fred C. Felter, editor of the *Pacific Drug Review;* John R. Bromell, of Curtis Publishing Co.; and John C. Davis of Davis Brothers Drug Co., Denver. A "Chuck Wagon" dinner was enjoyed at the summer home of President D. M. Kellam.

The North Carolina Pharmaceutical Association met in High Point May 16th to 18th. The attendance was good and a delightful program was enjoyed. Among the speakers were the following: C. C. Fordham, president; Dean R. B. House, University of North Carolina; Hon. Carl T. Durham, congressman; Dr. R. L. Swain, editor of *Drug Topics;* Dr. B. W. Kilgore, state chemist.

The New Mexico Pharmaceutical Association met in Carlsbad May 17th and 18th. An extensive business program was arranged, and among the speakers were: E. C. Welch, "Your Association;" G. H. Sasser, "Employer, Employee Relationship;" John W. Allen, "Additional Profitable Lines for Drug Stores;" Ralph A. Beegle, "The Complete Merchandising Campaign;" John Bromell, "Profits Through Display."

Howard College, Birmingham, Ala., held its Fourth Annual One-Day Drug Conference on May 12th. Among the speakers were: Dr. Seale Harris, "Drugs, Doctors, Dentists and Druggists;" Dr. Leo B. Dillon, "Opportunities in Dental Pharmacy;" Elbert W. Gibbs and Sam Watkins, "Fair Trade;" Dr. A. Richard Bliss, Jr., "The New Food, Drug and Cosmetic Law."

The Indiana Pharmaceutical Association met at Wawasee, June 13th to 15th. Theodore Christianson, former governor of Minnesota and now public relations counsel for the N. A. R. D., spoke on "Fair Trade." Jack I. LeVant discussed proper merchandising methods for retail drug stores. Dramatizing Pharmacy was the central theme of the professional session known as "Prescriptions Make Money." This session was conducted by four outstanding authorities: Harry S. Noel, Eli Lilly & Co.; Dr. Ralph W. Clark, Merck & Co.; Roscoe Carver, Kiefer-Stewart Co.; and J. W. Snowder, Pictorial Paper Package Co.

Minnesota Pharmaceutical Association met in Duluth on June 26th. A scientific section was conducted by Dean C. H. Rogers of the University of Minnesota and a merchandising section under the direction of President George T. Kermott. The business sessions were interesting and instructive and the entertainment features most enjoyable.

The South Dakota State Pharmaceutical Association met in Sioux Falls this year. The sessions were heavily attended and both business and entertainment programs left little to be desired. Among the speakers were: Theodore F. Christianson, former governor of Minnesota; "Trend of Legislation," Dr. R. L. Swain, editor of *Drug Topics;* Keith K. Keller, Minneapolis; John W. McPherrin, Chicago. C. A. Locke, Brookings, delivered the president's address. He reviewed the highlights of his administration and recommended continuance of an aggressive legislative program. Major J. P. Murphy delivered an interesting talk relative to the drug stores in Central American states. John J. McQueen discussed "Fair Trade for Profit."

Commencement Exercises of the Medical College of Virginia, Richmond, Va., were held

on June 6th. There were twenty-five graduates in Pharmacy. **Dr. Walter E. Vest,** an alumnus, was award the honorary degree of Doctor of Science. Dr. Otis W. Caldwell, general secretary of the American Association for the Advancement of Science, delivered the Commencement address. Baccalaureate sermon was given by Rev. George Ossman, in Monumental Church, June 4th.

Alpha Eta Chapter of Phi Delta Chi Fraternity, Wayne University, won the interfraternity scholastic trophy, the beautifully engraved silver cup. This award is made each year to the fraternity that has the highest general scholastic average. It is the ambition of Alpha Eta Chapter to break all precedents and become the proud owner of this coveted trophy by winning successively for three years.

The Utah Pharmaceutical Association met in Salt Lake City, May 22–24. Among the speakers were: Harry S. Noel, of Eli Lilly & Co., "The Bigness of Little Things;" John T. Witty, president of the N. A. R. D., "Looking at the Drug Business in 1939;" James DePree of DePree Co., "Taking the Mystery Out of Vitamins;" and an address on "The New Pure Food and Drug Law," by a representative of the U. S. Department of Agriculture. Among the entertainment features was a colored film, taken on a Colorado River expedition, shown by Dr. Russell G. Frazier, the explorer.

The Sixth Biennial Congress of the International Hospital Association will be held in Toronto, Canada, September 19–23, and all hospital workers in every land throughout the civilized world are welcome. An outstanding success is anticipated and all Hospital interests are coöperating to ensure every delegate a happy and instructive visit.

Mr. Arthur W. Steers, Fairchild Scholarship winner for 1938, recently was visited by Dr. Ray Clough of the National Canners' Association. Mr. Steers is working on Vitamin A and D content in canned salmon, for his Master of Science degree, which he expects to receive in June.

The Alabama Pharamaceutical Association met in Mobile on June 13–15. The convention was called "The Fair Trade Jubilee." Much enthusiasm was displayed and the meeting was one of the best ever held. Entertainment features included a Fair Trade Dinner and a "Jubilee Ball." Addresses on Fair Trade, Merchandising and Professional Pharmacy were enjoyed.

The Florida Pharmaceutical Association met at Hollywood Beach, May 16–18. Among the speakers were: Malcolm Hart, of Pepsodent Co.; I. H. Bander, McKesson & Robbins, Inc.; J. W. Snowden, Pictorial Paper Package Corp., "What Makes Prescription Business;" and Dr. B. V. Christensen of Florida School of Pharmacy, on "How the New Food, Drug and Cosmetic Law Will Affect the Retail Druggist." Entertainment was of the finest and the convention a very successful one.

The American Drug Manufacturers Association met at White Sulphur Springs, W. Va., May 2–4. The meeting was well attended and it was decided to hold next year's convention at the same place. Dr. John F. Anders, of E. R. Squibb & Sons, Mr. Carson P. Frailey, secretary of the Association, Dr. J. J. Durrett, technical adviser of the Food and Drug Administration, Dr. Paul N. Leech, secretary of the American Medical Association, addressed the convention. Mr. S. DeWitt Clough, of Abbott Laboratories, Chicago, was elected *President* and Mr. C. P. Frailey was re-elected as *Secretary*.

Among recent visitors at the American Institute of Pharmacy was **Pharmacist Etienge** of Verviers, Belgium, near Liége. Mr. Etienge was in attendance at the International Congress of Military Medicine and Pharmacy at the time.

Diplomas were awarded to eighty graduates of the College of Pharmacy of Columbia University on May 25th. Those exercises marked the completion of the 109th academic session of the College and the last commencement exercises that will be held by the institution as a separate entity. Hereafter all those graduated from the course will receive their degrees at the Columbia University exercises.

President Nicholas Murray Butler presided and made a short address of welcome, and the address to the graduates was delivered by the Honorary President of the College, Dr. Wm. Jay Schieffelin, whose great-grandfather was a trustee of the College.

A "perfect day" was had by all, on May 20th, when more than four thousand relatives and friends of employees of Merck & Co., Inc.,

Rahway, N. J., visited the main plant, research laboratories and offices of the Company. The occasion was a very special event known as "Employees' Day."

The Proprietary Association met in New York City, May 15th to 17th. Among the talks of interest was one by a representative of the Federal Trade Commission on "One Year of Enforcement under the Wheeler-Lea Amendments to the Federal Trade Commission Act." State and Federal legislation affecting the industry was also discussed.

On Saturday, May 20th, members of the graduating class of Philadelphia College of Pharmacy visited the American Institute of Pharmacy, en route to Eli Lilly & Co., Indianapolis, Ind., for an inspection trip. The group was accompanied by Prof. E. H. MacLaughlin of the College and Mr. Lee G. Cordier, of Eli Lilly & Co.

The District of Columbia Pharmaceutical Association met at Wardman Park Hotel, Washington, D. C., June 7th and 8th. Among the speakers were: Fred W. Irish, Food and Drug Administration, "Food, Drug and Cosmetic Law;" Maurice Protas, M.D., "Sale and Storage of Insulin;" Harry P. Dowling, M.D., U. S. Public Health, "Pneumonia Types;" B. R. Mull, "Prescription Department;" L. H. Ash, "The Changing Trend in Pharmacy;" H. Wales, Food and Drug Administration, "Food, Drug and Cosmetic Law;" Paul F. Dickens, M.D., "The Endocrines;" Dr. John C. Krantz, Jr., University of Maryland Medical College, "Chemistry and Pharmacology of Sulfanilamide;" Ralph Hayes, vice-president, Miller Drug Co., "Merchandising;" Dr. Samuel L. Hilton, "New Official Formulas, Elixir Phenobarbital, Syrup of Iron Iodide." The meeting, the first for some time, was well attended and a big success.

The New York State Pharmaceutical Association met in Richfield Springs, June 19th to 22nd, for the sixty-first time. The location was ideal, program interesting and the entertainment features splendid. Among the speakers were: Abraham Lichterman, acting director, Bureau of Food and Drugs, New York City, "Relation of the Pharmacist to the Advancement of Public Health;" I. H. Bander, vice-president, McKesson & Robbins, Inc., "Foot Traffic;" Nicholas S. Gesoalde, past president, New York State Pharmaceutical Association, "Fair Trade Enforcement in Other Retail Industries."

The 117th Annual Commencement of the Philadelphia College of Pharmacy and Science was held on Wednesday evening, June 7th, at 8:00 o'clock. The principal address was delivered by Dean Theodore A. Distler, of Lafayette College, on "Educating for Citizenship."

The New Jersey Pharmaceutical Association met in Atlantic City on June 27th, for the sixty-ninth time. The business meetings were interesting and instructive and the social features entertaining. Among the speakers were: former Governor H. G. Hoffman, now director of the New Jersey Unemployment Compensation Commission; Dr. J. Lynn Mahaffey, New Jersey State Director of Health; Mr. Thomas W. McGeever, of the Federal Narcotic Bureau; and Dr. William L. Sampson, of Rutgers University College of Pharmacy, who gave an instructive talk on "Some Recent Developments in the Field of the Vitamins." The drug exposition was excellent.

The 62nd Annual Convention of the Pennsylvania Pharmaceutical Association met in Johnstown June 19th to 22nd. The attendance was large, business sessions interesting and instructive and entertainment features good. Banquet and ball were held in the Masonic Temple with Dr. Ivor Griffith, dean of the Philadelphia College of Pharmacy and Science, as toastmaster. A memorial service was held on Thursday evening.

The Maryland Pharmaceutical Association met in Ocean City, Md., June 20th to 22nd. The commercial and professional programs were excellent. Among the speakers were: Dr. Neal Bowman, of Temple University, "Why Customers Are Lost;" John R. Bromell, "You Get Only What You Bid for;" Calvin Wheat, "Encourage the Amateur Photographer;" Dr. Wilton C. Harden, "Germicides and Antiseptics;" Kenneth A. Bonham, editor of *American Druggist*, "Seeing Is Believing;" Wm. Weber, Burroughs-Wellcome & Co., "Fair Trade from Manufacturing Point of View;" Howard W. Naulty, "Capture and Handling of Rattlesnakes for Breeding Purposes;" Dr. John C. Krantz, Jr., "New Drugs Admitted to the Second Supplement of the U. S. P. XI;" Herbert Levy, counsel, Maryland Pharma-

ceutical Association, "Some Aspects of Fair Trade Legislation;" Dr. H. C. Byrd, president, University of Maryland, "Our University;" Dr. C. W. Chapman, professor of Pharmacology, School of Pharmacy, University of Maryland, "Standards for Biological Assays." At the banquet Dr. R. L. Swain, editor of *Drug Topics*, was toastmaster; and the speakers were: Hon. Herbert R. O'Conor, Governor of Maryland; and Hon. Millard E. Tydings, United States Senator from Maryland.

Omicron Chapter of Rho Chi, Honorary Pharmaceutical Society, elected Dr. R. L. Swain to membership on May 9th, at its banquet at the Hotel Stafford, Baltimore, Md. The chapter was established at the School of Pharmacy of the University of Maryland in 1930.

The Veteran Druggists' Associations of Baltimore and the District of Columbia held their annual joint outing at Olney Inn on May 24th. There was a splendid attendance and the occasion was much enjoyed.

The annual banquet of the Alumni Association of the School of Pharmacy of the University of Maryland was held at the Lord Baltimore Hotel on May 31st. Dr. Charles L. Armstrong, '14, was toastmaster, and ex-Governor Harry W. Nice the principal speaker. The school orchestra in charge of Dr. F. J. Slama furnished the music.

Dr. W. G. Crockett, professor of Pharmacy at the Medical College of Virginia, was awarded the honorary degree of Doctor of Science by Hampden-Sydney College at the final exercises of that institution on June 6th.

The Department of Science of Johns Hopkins University, Baltimore, Md., arranged a testimonial dinner on May 19th in honor of **Dr. A. R. L. Dohme** who received his Ph.D. degree from the University in 1889. The dinner followed the last A. R. L. Dohme Lecture for 1938–1939, which were founded by Dr. Dohme, at which he spoke on, "Fifty Years of Chemistry."

Dean W. F. Rudd, School of Pharmacy, Medical College of Virginia, is the president-elect of the Virginia Academy of Science and will take office for one year during the next annual meeting to be held in Roanoke in May 1940. It is very encouraging to note the increasing number of pharmacists who are taking an active part in the state Academies of Science.

The Galen Pharmaceutical Society tendered a testimonial dinner to **Dr. J. A. Koch,** dean emeritus of the Pittsburgh College of Pharmacy, University of Pittsburgh, at the Hotel Schenley, Pittsburgh, on Thursday evening, May 25th, during which an oil portrait of Dr. Koch was presented to the College.

Dr. E. N. Meuser, Department of Pharmacy, West China Union University, Chengtu, Sceehwan, China, who has been in the United States and Canada on leave of absence since 1937, has returned to his duties. The four mission hospitals in the city and the newly erected Clinical Teaching Hospital are being combined to form the Chengtu United Hospitals and Dr. Meuser has been invited to take charge of the pharmacies in these hospitals including the procurement of medical supplies.

A special revision of the Japanese Pharmacopœia has been completed, after seven months work, by a commission of pharmacists headed by Dr. Keimatsu. The final meeting was held with the Japanese Pharmacopœia Investigation Commission.

A Department of Pharmacy has been established in Kyoto Imperial University and is welcomed because of a larger coöperation for Pharmacy.

The Virginia Pharmaceutical Association met at Virginia Beach, June 26th to 28th. Among the speakers were: Charles L. Guthrie, "Whither Bound?" Wm. G. Tarrant, Jr., "U. S. P. and N. F. Promotional Work in Virginia;" Prof. Marvin J. Andrews, University of Maryland School of Pharmacy, "Interprofessional Relations Work in Maryland;" Theodore Christianson, N. A. R. D., Chicago; Dr. P. B. Dunbar, "The Federal Food, Drug and Cosmetic Act from the Regulatory Officers' Viewpoint."

Dr. H. C. Christensen received an Honorary Degree of Doctor of Science from the New Jersey College of Pharmacy at the annual Commencement on Wednesday, June 7th.

Chairman John F. O'Brien of the Committee on Pharmacy Week has announced that the fifteenth observance of National Pharmacy Week will be held during the week of October 22nd to 28th. Further details will be announced as the program develops.

Dr. Lewis E. Jarrett, states in *Hospitals* for June 1939, "The pharmacy is a 'forgotten' de-

partment in many hospitals and yet it is one of the most important units and one that has many possibilities. Every hospital of fifty beds or more should consider the development of the pharmacy or adequate and safe pharmaceutical service, both for the patients and for the staff, as well as for its economic value to the hospital. Smaller hospitals may assign additional duties to the pharmacist, who after all is a well-trained person, capable of rendering a variety of services."

Louisiana State Pharmaceutical Association held its 57th convention in Alexandria on May 17th and 18th. One of the highlights of the program was an open forum on "Fair Trade and Its Benefits." Among those taking part in the discussion were: H. L. Richardson, Shreveport; John J. Spatafora, Monroe; C. R. Caldwell, Shreveport; and Harold A. Dempsey. One of the outstanding speakers at the meeting was Dean C. Leonard O'Connell of the Pittsburgh College of Pharmacy.

The 60th annual convention of the Texas Pharmaceutical Association met in Dallas on June 5th to 8th. The following addresses were heard: Hon. R. L. Reader, "Your Legislature;" Charles Foster, New York City; Walter Quinlan, "Are Retailers Responsible for Policies of Manufacturers?" Hon. J. Franklin Spears, senator; Dr. R. L. Swain, editor of *Drug Topics*, "Your Pharmacy and Mine;" Dean W. F. Gidley, College of Pharmacy, University of Texas; Marshall Searcy, president 1939 Senior Class, College of Pharmacy, University of Texas; I. H. Bander, McKesson & Robbins, Inc., New York City, "More Feet—More Profits;" Malcolm Hart, "Advantages of Fair Trade to the Retail Drug Industry;" James L. Freeman, "What Do Retailers Owe to Manufacturers Who Have Stabilized Prices?"

Arkansas Pharmaceutical Association met in Little Rock, June 13th to 15th. Among the addresses were: "The Business Commandments of a Good Merchant," E. D. Stribley, McKesson & Robbins, Memphis; "Better Lighting," James F. Tuohey, Arkansas Power & Light Co.; "Drug Store Arrangement," Jim De Pree, De Pree Chemical Co.; "Measuring Consumer Opinion," L. L. Shoemaker, National Cash Register Co.; "Interprofessional Relations," B. R. Mull, Eli Lilly & Co.; "Highlights and Shadows," W. C. Campbell, Eastman Kodak Co.; "How to Win Friends and Influence People," Dale Carnegie.

Dr. and Mrs. John G. Beard, of the School of Pharmacy, University of North Carolina, attended the recent Commencement Exercises at the U. S. Naval Academy, Annapolis, Md., to witness the graduation of **John Grover Beard, Jr.**, who was a recipient of many honors.

Louis H. Roddis, Jr., recently graduated from the United States Naval Academy at the head of his class. Mr. Roddis is a son of Comdr. Louis H. Roddis now stationed in Honolulu, and who has been a member of the ASSOCIATION for many years.

The Japanese Memorial Society prepared for a memorial celebration in honor of the late Dr. Hideyo Noguchi. It was intended to invite Ambassadors from various countries including Great Britain and the United States. This celebration took place on May 21st.

James A. Donovan, retail pharmacist of Buffalo, N. Y., received the Gregory Memorial Medal of the Pharmacy Alumni Association of the University of Buffalo at the recent association banquet. The medal was established as a memorial to the late Dr. Willis G. Gregory. It is to be given annually to some outstanding pharmacist of Western New York who personifies the ideal of service and integrity in the pharmacy profession.

In the *Industrial and Engineering Chemistry* for May 1939, on page 531, appears a most interesting article entitled, "The American Way in Pharmacy," by Dr. George D. Beal of Mellon Institute for Industrial Research, University of Pittsburgh, Pittsburgh, Pa.

The Kentucky Pharmaceutical Association met at Lexington, June 13th to 16th. Among the speakers were: Warren P. Boulton, secretary, Department of Professional Regulations; Dr. G. L. Curry, dean, Louisville College of Pharmacy; O. B. Capelle, Sales Promotion Manager, Miles Laboratories; James De Pree, Sales Manager, The De Pree Co.; Rowland Jones, Jr., Washington Representative of the National Association of Retail Druggists; W. C. Burrow, Commissioner of Industrial Relations.

Victor Kebler, Jr., grandson of Dr. and Mrs. Lyman F. Kebler, and an Eagle Scout, presented King George VI, on his recent visit to Washington, D. C., a neckerchief slide decorated with a shark's tooth, the emblem of the Washington Boy Scouts.

OBITUARY.

FRANK M. McCABE.

Mr. Frank M. McCabe, vice-president of the Bruce Publishing Co., St. Paul, Minn., editor of the *North Western Druggist* and secretary of the Northwest Pharmaceutical Bureau, died suddenly on May 19th, at his home, having been at his desk a few hours before.

Born in Hopedale, Ill., fifty-four years ago, Mr. McCabe came to Minnesota in 1913. He was employed by the Northern Pacific Railroad, but this service was interrupted by the World War, in which he saw fifteen months service overseas, being Captain in the Signal Corps, 89th Division. He returned to the Northern Pacific and remained until 1919, when he joined the Bruce Publishing Co., where he leaves a vacancy which will be difficult to fill.

As editor of the *North Western Druggist* he was known from coast to coast in pharmaceutical circles, and in no small measure contributed to the growth and development of the drug industry.

Burial was in Fort Snelling National Cemetery. His widow, Mrs. Emily Quinn McCabe, survives.

CHARLES H. MAYO.

Dr. Charles H. Mayo, honorary member of the AMERICAN PHARMACEUTICAL ASSOCIATION, died May 26th, in Chicago, in his 74th year. Mrs. Mayo and members of the family were with him when the end came, and the train bearing his remains was met at the station in Rochester, Minn., by quite a large delegation of the citizens. The day of the funeral all activities were suspended for some hours. Dr. Mayo was a native of Rochester and he and his brother, Dr. William J. Mayo, ran the famous Mayo Clinic.

Few parts of the world have not heard of the city of Rochester because of the wonderful work of the Mayo family. Soon the suffering began to find their way to Rochester from all parts of the Northwest, and little by little from other parts of the country, and each patient was asked to pay what he could afford and no more, and if he could afford nothing, his bill was receipted just the same. Money poured in upon the brothers but all of it, above a small margin of safety, was applied to the fund that in 1915 was turned over to the Mayo Foundation.

All over the nation are graduates of the Mayo Foundation, famous specialists, acting in accordance with the ideals of their teachers. Perhaps its greatest service of all has been in the field of medical research and hardly a year has gone by that it has not contributed a major discovery for the relief of human suffering and the prolongation of human life.

Thus Dr. Mayo passes, after a lifetime of service to his fellowmen hardly to be matched in his generation.

BOOK NOTICES AND REVIEWS.

Advances in the Therapeutics of Antimony, by PROF. DR. HANS SCHMIDT, Ph.D., and DR. F. M. PETER, M.D. Preface by DR. PHILIP MANSON-BAHR. Publishers, George Thieme, Leipzig, Rossplatz 12. Price, paper 18 R.M., bound 19.50 R.M.

This review gives an opportunity of quoting a definition for the word "chemotherapy." This has been defined as "the study of the action of molecules of definite structure upon protoplasm which involves the assumptions that certain radicals have a selective affinity with parts of the cells."

Interesting history is associated with Antimony, not only by women to embellish their beauty but its preparations were ranked high by Basil Velentine, Paracelsus and others; emetics were largely used—"many vomited to eat and ate to vomit." Antimonial cups were in favor and a "perpetual fill" was employed; cuts were decorated indicating the favor in which Antimony was held; in substance and insignia proclaimed that "it was a wonder of nature and for all men a certain cure." It was also employed as a poison.

Two hundred and sixty pages are required in giving the history and the study of the advances of a useful drug in its applications for diseases of man and animals; sometimes exalted and its use for periods prohibited, and now again has a place in modern Medicine and employed in parasitic diseases, kala-azar, etc. The results of the treatments are favorable, and the authors have contributed an extensive research which may result in more successful treatments of Ponos, kala-azar and related diseases, in which antimony has been employed.

The Handmaiden of the Sciences, by ERIC TEMPLE BELL. 216 pages. Published by Williams & Wilkins, Baltimore, Md. Price, $2.00.

Die Arzneikombinationen, von PROFESSOR DR. EMIL BÜRGI. 28 illustrations. Publishers, Julius Springer, Berlin.

The many names of compound medicinal preparations, chemicals, etc., has been a burden for physicians and pharmacists. A purpose of the book is to acquaint these with the compounds. Some of the compositions have for the first time been revealed in a publication. There are about 170 pages. Price, 12 R.M. In the Introductory, the author outlines his plan of discussion and in the effort he presents individual action of the components and the response of the organs The historical study refers to the period, long ago, when the therapy consisted chiefly of complicated mixtures; many of the narcotics were compounds of several, as ether, chloroform, morphine, or of digitalis, atropine and other additions. The author presents a general discussion and treats of the constituents and their action. Cannabis is given attention, the newer chemicals and drugs; in this the effect is studied at length. If the materia medica is employed, it should be understood and the effect on the system, some of the misuses would then be avoided. In a concise way this is stated in the lines of page 55, where he emphasized the fact that "additions may produce undesired effects with the desired" and this caution appears in connection with the careful study throughout the book in the presentations on ailments and of agents for the medical treatments. The book will be found valuable in the library of the physician, the pharmacist and of related groups.

Methods for Analysis of Medical Specialties, Second Edition of the Kommision des Internationalen Apotkerbundes (Society). Federation Internationale Pharmaceutique, Leyden. Buchhandlung Dekker en Nordemann N. V., Amsterdam. Price, $3.50. The Specialties Commission is composed of: Prof. Dr. Van Italie, chairman; Dr. H. Baggesgard, secretary; Dr. A. Rising; Dr. E. Weiss; Prof. Dr. P. Casparis; Dr. E. Höst Madsen; Prof. Dr. C. A. Rojahn (deceased) was a member. Coöperation is invited.

There are about 150 pages, including a number of Tables, one from Netherlands Pharmacopœia and that of the Table for Conversion of Saybolt or Engbro viscosity into timematic viscosity, of the U. S. P., page 477. The methods are published in German; they include the determination of melting point, boiling point, alcohol, ash, rules for carrying out reactions, etc. The use of the book in this country, will be limited largely to the laboratories and schools; its standing as authority, is sponsored by the compilers, who are well and favorably known.

Fundamentals of Experimental Pharmacology, by TORALD H. SOLLMANN, M.D., Sc.D., Professor of Pharmacology and Materia Medica, and Dean of School of Medicine, Western Reserve University, Cleveland, Ohio; Chairman Council on Pharmacy and Chemistry, American Medical Association; Author, "A Manual of Pharmacology," Fifth Edition, 1936; and Paul J. Hanzlik, A.M., M.D., professor of Pharmacology, Stanford University School of Medicine, San Francisco; Vice-Chairman, Council on Dental Therapeutics, American Dental Association; Editor, "A Handbook of Accepted Remedies, Symptoms and Treatment of Poisoning, etc.," Second Edition, 1917.

This is the Second Edition and illustrated, J. W. Stacy, Inc., San Francisco, 1939. Price, $4.25. The revision was made by the junior author, who assumes the responsibility for errors and omissions. The reviser states that the manifold requirements of medical science, public health, industry and governmental agencies have increased the opportunities and responsibilities of the pharmacologist. The book provides a course of practical exercises and testing methods. Part I includes Chemical Pharmacology and Part II Experimental Pharmacodynamics; fifteen chapters treat the first and thirteen the second, and thirteen appendix divisions including the arrangement of the department.

Chapter I considers Plant Constituents in Sections A to J. Chapter II Liquid Pharmaceutical Preparations under Sections A to K. Chapter III includes Solid Pharmaceutical Preparations in eight sections. Chapter IV discusses colors, flavors, incompatibilities, metrology and prescription writing. Chapters V and VI include important and poisonous drugs and VII antidotes. Other phases of the effects of drugs are discussed in succeeding chapters, their executions and tests for them, dosage by various administrations and conditions of the patients, the test animals, anesthetized and otherwise.

The book is a useful addition to the library and for review by the students of both medical and pharmacy schools. The arrangement is systematic and adapted for ready reference. Pharmacists will find the book a guide at the Prescription Desk, helpful to the writer, and for the teacher comprehensive notes and directions for his lectures.

ACIDITY OR p_H STANDARDS.

For some time the Bureau of Standards, U. S. Department of Commerce, has been urged to undertake the development of acidity or p_H standards, test and control methods and calibrations, in order to place this very important method of control on a uniform and, therefore, more comparable basis.

The officials of the Bureau of Standards have recognized the importance of the proposal and have agreed to coöperate in establishing the desired standards.

Representatives of several interested professions, sciences and industries, including the AMERICAN PHARMACEUTICAL ASSOCIATION, have supported the request of the Bureau of Standards for the funds required to secure the necessary equipment, supplies and personnel and to carry on the experimental work involved.

These representatives recently appeared before sub-committees of the Committees on Appropriations of the House of Representatives and the Senate and were apparently successful in impressing on the members the value of p_H measurement and the importance of having the proposed standards established.

It is now assured that the program will be started early in July and carried through as promptly as is possible. The Bureau of Standards is to be complimented on the splendid response to this request for aid in developing standards in another important field of measurement.—E. F. K.

TECHNICAL COMMISSION OF PHARMACOPŒIAL EXPERTS.

THE LEAGUE OF NATIONS.

A meeting was held at Geneva, May 10th to 16th. Dr. Hampshire, London, presided and there were present Professors: Baggesgaard-Rasmussen, Copenhagen; Eder, Zurich; Fullerton Cook, Philadelphia; van Itallie, Leyden; Tiffeneau, Paris; and Zunz, Brussels.

The chairman reported that the Reference Sub-Committee on Galenical Pharmacy had been duly constituted since the last meeting and had made some progress with the work of defining general methods of preparation and of unifying formulas.

The Commission revised and extended a draft of the "General Notices" containing descriptions of general tests and methods, together with explanations of the terms and modes of expression to be employed in all monographs.

Drafts of 85 monographs which had been prepared by members of the Commission since the last meeting, were presented for consideration. These were classified into groups of similar substances, such as: alkaloidal salts; crude drugs; the digitalis group; mercurial compounds; the ergot group; general organic chemicals. Certain monographs from each group were selected for detailed discussion. Arrangements were made for the preparation of new drafts in accordance with the decisions taken in relation to the individual monographs.

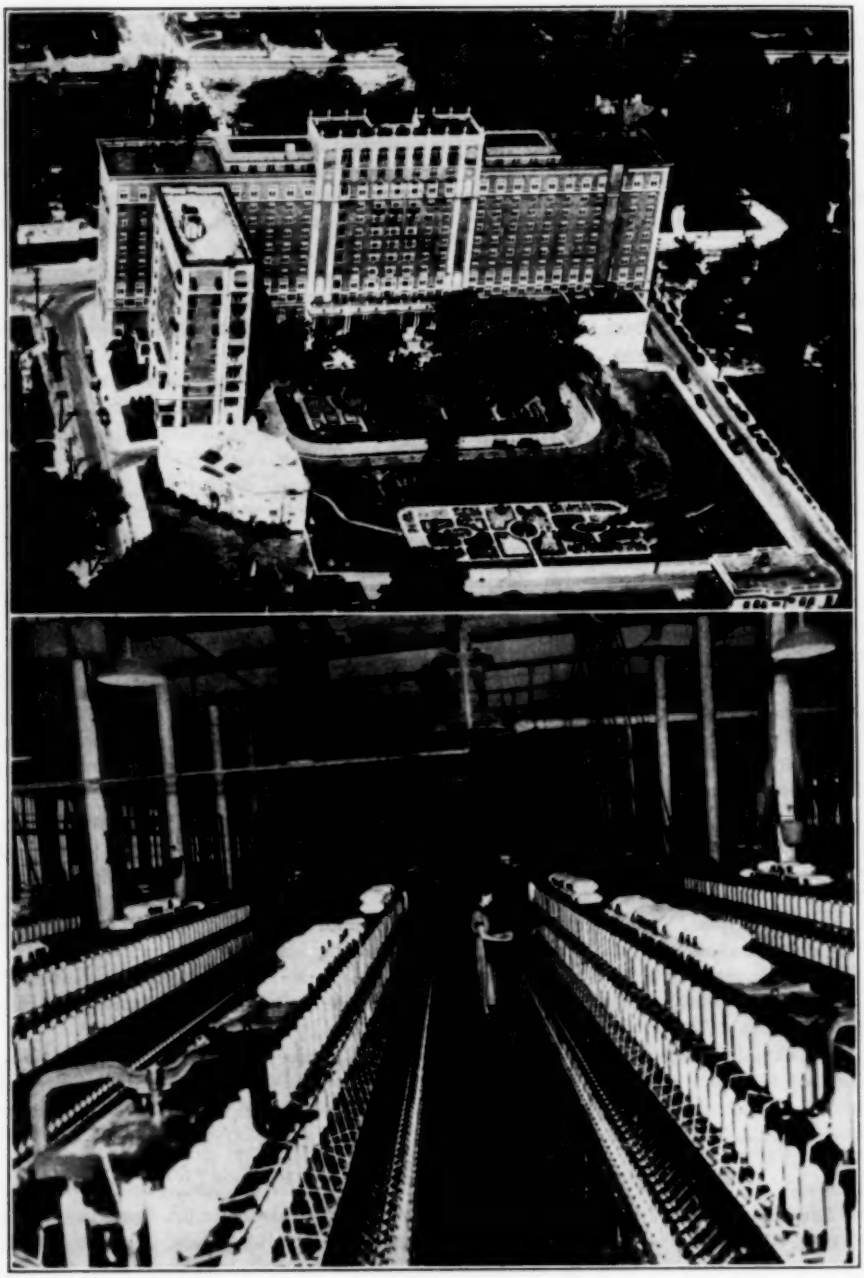
In the course of the discussions various problems presented themselves for investigation and the members of the Commission formed themselves into small groups for the investigation of specific problems.

Individual members undertook to report on other subjects, such as: the terminology relating to solubilities; thermometers; standards for color and absence of turbidity; limit tests for heavy metals and other inorganic impurities; sterilization of solutions for injection; neutrality reactions of alkaloidal salts; various solubilities of alkaloids, etc.

INTERNATIONAL PHARMACEUTICAL FEDERATION.

The International Pharmaceutical Federation will convene in Berlin, Germany, August 27 to 30, 1939. German pharmacists consider Pharmacy as a most important public health service. The program will bring home to the visitors the position of the German pharmacists and also will bring them in touch with the German governmental bodies. The program provides for a reception of the press and a visit to the tomb of the unknown soldier to place a wreath in memory of comrades who died on the battlefields. The members will attend the official opening of the Kroll Opera.

On August 28th a scientific program will be carried out; August 29th will be "Practical Pharmacy Day," especially of galenical pharmacy. The evening reception of the Reich government is expected to be a feature and the next day will be devoted to a discussion of the administration of Pharmacy in various countries. August 31st will be given to excursions to beauty spots of Germany. It is hoped that those who attend the meeting will write the Organizing Committee for the F. I. P. (International Pharmaceutical Federation) in Berlin-Charlottenburg 2, Carmerstrasse 3, so that programs may be sent them, prior to arriving at the Meeting.



Top, Biltmore Hotel, Atlanta, Ga. Convention headquarters for the 87th Annual Meeting, AMERICAN PHARMACEUTICAL ASSOCIATION, August 20th to 26th. This is a rear view of the famous hostelry showing the beautiful terraced gardens and grounds where some entertainment features of the coming convention will be staged, including the Georgia Barbecue.

Bottom, A Georgia Cotton Mill. Visitors at the Convention will be privileged to inspect a Cotton Mill.